TO STUDY THE EFFECTIVENESS OF THORACIC PARAVERTEBRAL BLOCK VERSUS SYSTEMIC OPIOIDS FOR RELIEF OF POSTOPERATIVE PAIN IN PATIENTS UNDERGOING MASTECTOMY UNDER GENERAL ANAESTHESIA

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CERTIFICATE

This is to certify that this dissertation titled **"TO STUDY THE EFFECTIVENESS OF THORACIC PARAVERTEBRAL BLOCK VERSUS SYSTEMIC OPIOIDS FOR RELIEF OF POSTOPERATIVE PAIN IN PATIENTS UNDERGOING MASTECTOMY UNDER GENERAL ANAESTHESIA"** has been prepared by **Dr. L.SANJIV** under my supervision in the Department of Anesthesiology, Government Kilpauk Medical College, Chennai-10 during the academic period 2010-2013 and is being submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the University regulation for the award of Degree of Doctor of Medicine (M.D Anesthesiology) and his dissertation is a bonafide work.

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ABSTRACT

AIM OF THE STUDY

To Study The Effectiveness Of Thoracic Paravertebral Block Versus Systemic Opioids For Relief Of Post Operative Pain In Patients Undergoing Mastectomy Under General Anaesthesia.

AUTHOR : Prof.S.Gunasekaran,M.D.,D.A.,DNB

BACKGROUND

The incidence of acute postoperative pain in patients undergoing surgery for breast cancer is approximately forty percent. The conventional anaesthetic technique for management of a breast lump has been general anaesthesia and post operative pain relief by opioids. However, the incidence of side effects such as postoperative nausea and vomiting, pain are unacceptably high. To circumvent this problem a number of alternatives were tried. A very successful one among them is the thoracic paravertebral block. It is also considered technically simple and equally efficacious in relieving post operative pain when compared to epidural blocks with lesser incidence of side effects.

MATERIALS AND METHODS

We performed this study after getting institutional ethical committee approval (Government Kilpauk Medical College). This study was performed in adult women aged 18-60 years with Body mass index from 18.8 -24.0 belonging to American Society of Anaesthesiologists ASA 1and2 undergoing elective modified radical mastectomy under general anaesthesia.

Group A :

Twenty five patients receiving standardized general anaesthesia for surgery with thoracic paravertebral block (0.3 ml / kg or 1.5 mg / kg of 0.25%. Bupivacaine at levels T3 and T5) for postoperative pain relief.

Group B :

Twenty five patients receiving standardized general anesthesia for surgery with systemic opioids. All patients received injection tramadol 100 mg intravenously for post operative pain relief.

Post operatively the following parameters were noted and taken for statistical analysis, time duration of complete analgesia, duration of effective analgesia, hemodynamic stability, PONV incidence, sedation , type of rescue analgesia and time, incidence of pneumothorax by checking air entry/X-RAY.

RESULTS

The mean duration of complete analgesia(VAS score of zero)in group A(study group)is 70 minutes and in group B(control group) is 35.5 minutes which is statistically significant.Hence the time duration of complete analgesia is significantly higher in the thoracic paravertebral block patients. The mean time duration of effective analgesia(VAS<4) in group A(study group)is 308.71 minutes and in group B (control group) is 144.26 minutes which is statistically significant.Hence the time duration of effective analgesia is significantly higher in thoracic paravertebral block group (group A). The need for rescue analgesia in group A(study group) is nil,while in group B(control group)seven out of twenty five patients required rescue analgesia. The incidence of PONV in group A(study group)is nil,while in group B(control group),ten out of twenty five patients reported PONV. Hence,the incidence of PONV is significantly lower in thoracic paravertebral block group.

CONCLUSION

This study concludes that thoracic paravertebral block provides a better postoperative analgesia,stable hemodynamic status,,nil incidence of postoperative nausea and vomiting,and overall better comfort for the patients undergoing mastectomy under general anaesthesia than systemic opioids.(injection tramadol)

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DECLARATION

I, Dr. L.SANJIV, solemnly declare that the dissertation , **"TO STUDY THE EFFECTIVENESS OF THORACIC PARAVERTEBRAL BLOCK VERSUS SYSTEMIC OPIOIDS FOR RELIEF OF POSTOPERATIVE PAIN IN PATIENTS UNDERGOING MASTECTOMY UNDER GENERAL ANAESTHESIA"** is a bonafide work done by me in the Department of Anesthesiology and Critical care, Government Kilpauk Medical College, Chennai under the guidance of **Prof.Dr.S.Gunasekaran,** M.D.,D.A.,DNB Professor and HOD, Department of Anesthesiology, Government Kilpauk Medical College, Chennai-10

Place: Chennai Signature

Date: **(L.SANJIV)**

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CONTENTS

INTRODUCTION

The incidence of acute postoperative pain in patients undergoing surgery for breast cancer[1] is approximately forty percent. The conventional anaesthetic technique for management of a breast lump has been general anaesthesia and post operative pain relief by opioids. The detrimental effects of inadequate post operative analgesia and the resulting human response to it is well documented. The present strategy for pain relief is a multimodal approach. However, the incidence of side effects such as postoperative nausea and vomiting, pain are unacceptably high. To circumvent this problem a number of alternatives were tried. A very successful one among them is the thoracic paravertebral block.

The anatomical definition of the paravertebral space was defined in the beginning of the twentieth century. The first successful block was performed by Hugo Sellheim of Leipzig in 1905.Arthur Lawen was the first to map the pain pathways of thoracic viscera. However with the introduction of epidural analgesia and pharmacological advancements in general anaesthesia ,it went into a sleeping period. It staged a comeback in 1979 when Eason and Wyatt inserted a catheter in the paravertebral space and allowing possibility of repeated injections. It is also considered technically

simple and equally efficacious in relieving post operative pain when compared to epidural blocks.

With this background, this study was conceptualized to study the effectiveness of thoracic paravertebral block versus systemic opioids (injection tramadol intravenously) for relief of postoperative pain in patients undergoing mastectomy under general anaesthesia.

MODIFIED RADICAL MASTECTOMY

- Mastectomy[2] is the medical term for the surgical removal of one or both breasts.

- It is performed either to treat or to prevent breast cancer.

- There are three main types:

1) Simple or total mastectomy: Removal of entire breast tissue but does not remove the muscle tissue or lymph nodes under the breast.

2) Modified radical mastectomy: This combines a simple or total mastectomy, including the skin of the nipple and the areola, and includes removal of most of the lymph nodes in the armpit. It further has three types : Patey's mastectomy, Auchincloss mastectomy and Scanlon's mastectomy. Pectoralis minor is removed in the former two, while it is retracted in the latter.

3) Radical mastectomy - the removal of the breast, lymph nodes and chest muscles. This is no longer common.

- Severe acute pain after mastectomy is usually due to retraction, resection of skin over the breast tissues, injury to the underlying nerves, especially in the dermatomes T2 to T6.

- Inadequate management of pain in post mastectomy patients has major respiratory consequences, as inspiration is limited by pain which leads to reflex contraction of expiratory muscles and consequently to diaphragmatic dysfunction resulting in decreased FRC and atelectasis.

- Deep breathing requires stretching of the incision site which is extremely painful. Patients without adequate analgesia try to prevent stretching of the skin incision by contracting their expiratory muscles, thus limiting the stretch on the incision during inspiration.

- This failure to inspire deeply before a forceful exhalation results in ineffective cough, which in turn promotes retention of secretions, leading to airway closure and atelectasis. Diaphragmatic contraction is also impaired.

- Thus proper control of post-mastectomy pain, in addition to providing comfort for the patient, facilitates chest physiotherapy, effective expectoration and early ambulation.

- Various methods of post-mastectomy pain relief are available but none has matched the requirement of an ideal pain relief technique. Regional techniques are widely used nowadays because they are associated with less sedation and early ambulation.

- Thoracic epidural is considered to be the one of the accepted techniques for post-mastectomy pain relief and is used in selected centers. However the incidence of hypotension and other adverse side effects is quite high. As an alternative thoracic paravertebral block with equivalent analgesia and less incidence of side effects is fast regaining popularity.

PHYSIOLOGY OF PAIN[3]

PAIN

International Association for Study of Pain has defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or defined in terms of such damage.

There are two components of pain. Neuro physiologically mediated sensory component and an emotional component.

There are two types of pain

1. Acute pain - Acute pain is provoked by a specific disease or injury, serves a useful biologic purpose, is associated with skeletal muscle spasm and sympathetic nervous system activation, and is self-limited.

2. Chronic pain, in contrast, may be considered a disease state. It is pain that outlasts the normal time of healing, if associated with a disease or injury. Chronic pain may arise from psychological states, serves no biologic purpose, and has no recognizable end-point.

There are two major theories of pain.

1. Specificity theory proposed by von Frey states that pain is due to stimulation of specific end organs.

2. Intensive / summation / pattern theory proposed by Gold Scheider states that there are no specific pain receptors and any sensory stimulus if sufficiently severe would produce pain.

ORGANISATION OF PAIN PATHWAYS:

According to the recent theory, pain pathway is organized as follows (figure 3,4)

RECEPTORS:

Nociceptive receptors are fine, profusely branched, free nerve endings covered by Schwann cells with little or no myelin. They are present in skin, viscera and other organs.

There are three types of receptors

1. Mechanosensitive nociceptors activated by mechanical stimuli.

2. Mechanothermal nociceptors activated by mechanical and thermal stimuli >43ºC.

3. Polymodal pain receptors respond to mechanical, thermal and chemical stimuli like hydrogen and potassium ions, histamine, serotonin, bradykinin, prostaglandins and substance P.

FIRST ORDER NEURONS:

Mechanosensitive and mechanothermal pain receptors transmit impulses through thinly myelinated A delta fibres of 1-5 µ diameter with conduction velocity

FIGURE-3.PAIN PATHWAY

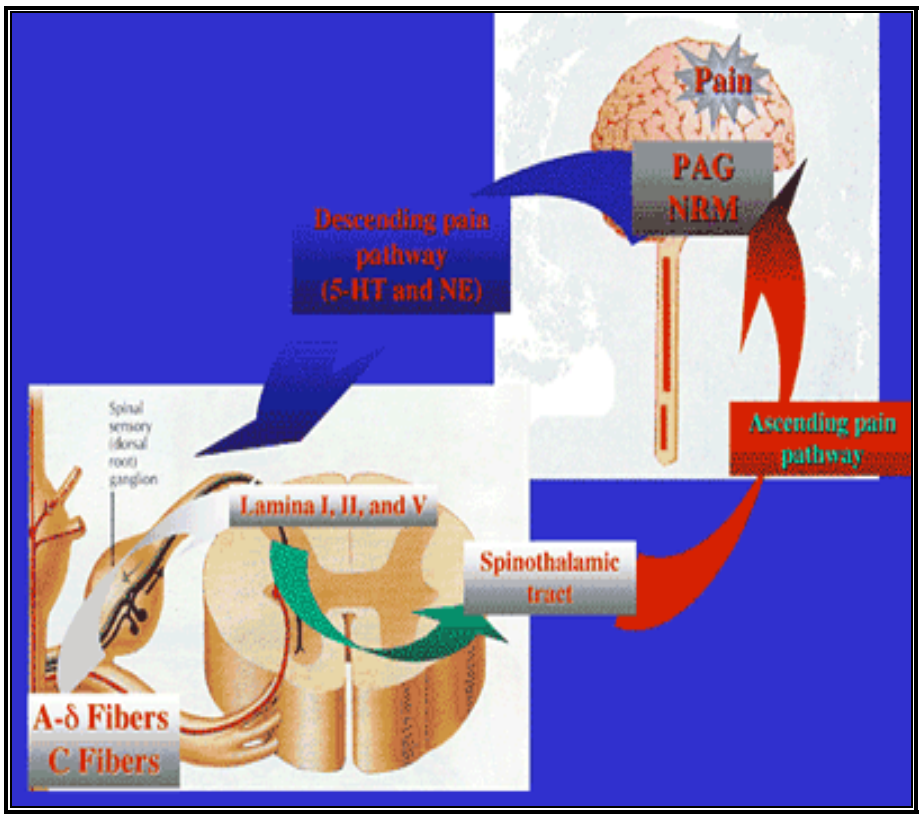
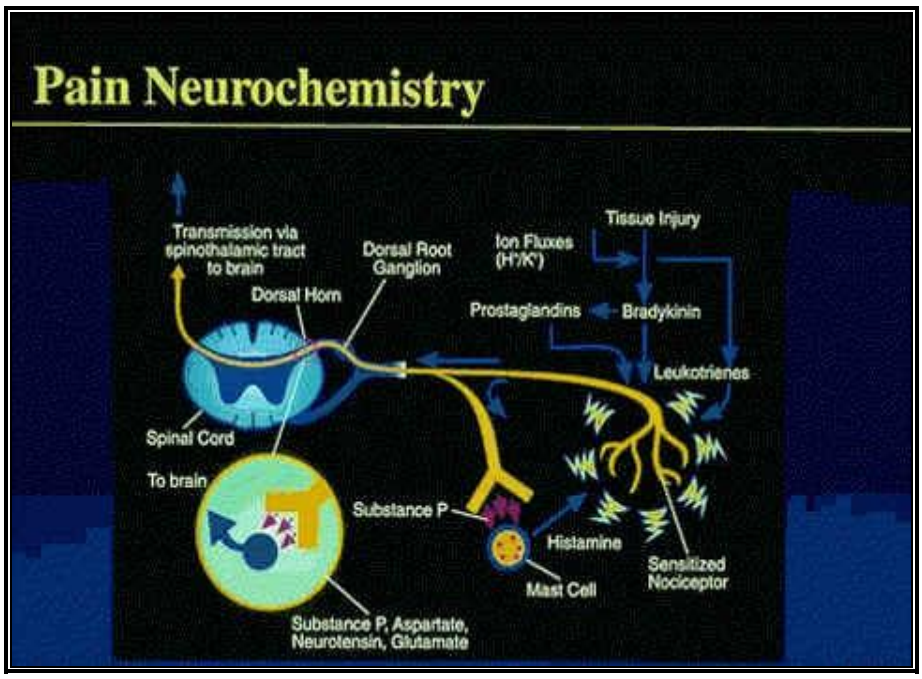


FIGURE.4.



of 15-30 metres per second. This is responsible for fast pain which is sharply localized. Polymodal pain receptors transmit impulses through unmyelinated C fibres of 0.4-1.1 µ diameter with conduction velocity of 0.5 – 2 meters per second.

This is responsible for the poorly localized slow pain. Transmission through both these fibres causes the " Double response of Lewis".

The peripheral afferent fibres have their cell body in the dorsal root ganglion and project via the lateral part of the dorsal root called " Tract of Lissauer". They terminate in dorsal horn of spinal cord within 1 to 2 segments of entry.

A delta fibres terminate in lamina 1 (marginal cell layer of Waldeyer) and lamina 5(wide dynamic range of neurons which respond to other modalities also). Unmyelinated C fibres terminate in lamina 2 & 3 (substantia gelatinosa).

SECOND ORDER NEURONS :

They arise from the cell and connect with ventral and lateral horn cells in the same and adjacent spinal segments and subserve both somatic and autonomic reflexes. Around 75% of other sensory neurons project contralaterally after decussating in the anterior commissure 1-3 segments higher than the root of entry and divide into two ascending tracts.

Neospinothalamic / Laternal spinothalamic tract: It ascends in the anterolateral funiculus of spinal cord to brain stem and thalamus and contains fast conducting fibres which transmit specific localised pain, identifiable in quality and intensity causing " First Pain ". The fibres are arranged in such a way that fibres from lower part of the body are superficial and from upper part of the body are innermost.

Palaeospinothalamic/Ventral spinothalamic/Spinoreticulothalamic tract:

It is medially placed and contains slowly conducting fibres responsible for " Second Pain" and has connections with reticular core or brainstem, limbic and subcortical regions.

Thalamic terminus: Most of the fibres of spinothalamic tract terminate in the nucleus ventro posterolateralis which is the major sensory relay nucleus. The other fibres terminate in the posterior group of nuclei, ventrobasal complex and hypothalamic nuclei.

THIRD ORDER NEURONS / THALAMOCORTICAL PROJECTIONS:

Posterior thalamic nuclei project to the post central cortex and upper bank of sylvian fissure and subserve tactile and proprioceptive stimuli with discriminative sensory function. Pain afferents received from mesencephalic offset of anterolateral funiculus project to the amygdaloid nuclei and other areas related to affect the emotion.

PERCEPTION OF PAIN :

The threshold for the perception of pain is the lowest intensity of stimulus recognized as pain. The conscious awareness or perception of pain

occurs at the thalamic level and thalamic pain occurs when the thalamocortical pathway is destroyed. Somatosensory cortex is essential for the accurate localization, appreciation of intensity and other discriminative aspects of pain. Prefrontal cortex subserves the unpleasant affective and emotional reaction to pain.

GATE CONTROL THEORY OF PAIN:

It was propounded by Melzack and Walls in 1965. It states that modulation of pain impulses in the dorsal horn can control further synaptic transmission via the spinothalamic tract. It states that stimulation of large afferent fibres (myelinated) excite the I cells (inhibitory cells) in the lamina 2 and 3 of dorsal horn which in turn cause pre and post synaptic inhibition of secondary transmission neurons(T cells) in lamina 5 of dorsal horn and interrupt pain pathway. Conversely stimulation of small pain afferents (C fibres) inhibit the I cells leaving the T cells in the excitatory state thus facilitating transmission of pain.

CENTRAL SENSITISATION:

Prolonged nociceptive stimulation leads to hyperexicitability of dorsal horn cells and increased cephalad transmission resulting in increased pain sensation. This is responsible for chronic pain syndromes. There are two

mechanisms for this chronic pain syndromes. Descending inhibitory pathways and endogenous pain control mechanisms. Endogenous neuronal system of analgesia was described by Renolds in 1969. It extends from the hypothalamus along the peri ventricular and periaqueductal grey matter which communicates through dorsolateral funiculus to end in the nucleus raphe magnus and locus ceruleus. Stimulation anywhere along this tract releases endogenous opioid like peptides called endorphins which activate serotoninergic pathways via descending reticulobulbar spinal system and interact with lamina 1 and 2 of the dorsal horn and exert analgesia. Another descending inhibitory pathway arises from locus ceruleus in Pons and projects directly to spinal cord. Here the neurotransmitter is noradrenaline and this pathway inhibits pain responses in spinal cord by Alpha 2 adrenergic mechanisms.

Endogenous opioids and other neurotransmitters and spinal modulation of pain perception:

Hughes et al described endogenous morphine like substances with analgesic activity called endorphins. There are 5 endorphins, **Metenkephalin, Leuenkephalin, Betaendorphin**, **L endorphin and R-endorphin**.

Metenkephalin and Leuenkephalin: They are inhibitory neurotransmitters at the primary afferent nociceptive site. They act through release of substanceP.

Dynorphins: Control nociception at the spinal cord level through activation of kappa receptors. It is present in lamina 1 to 5 of dorsal horn.

L-endorphin and R- endorphins are breakdown products of beta endorphins.

Substance P(Substance preparation): It is a 11 amino acid peptide. It acts as an excitatory transmitter in lamina 1,2,4 and 5 of dorsal horn, spinal trigeminal nucleus and type B cells in dorsal root ganglia. It is released in vivo by the activity of A delta and C fibers. Endogenous opiates inhibit presynaptic release of substance P. Serotonin released from descending inhibitory pathways inhibit the action of substance P at the post synaptic level thus inhibiting pain transmission.

Somatostatin: It is a 13 amino acid peptide found in lamina 2 of dorsal horn and inhibits function of afferent pain fibres.

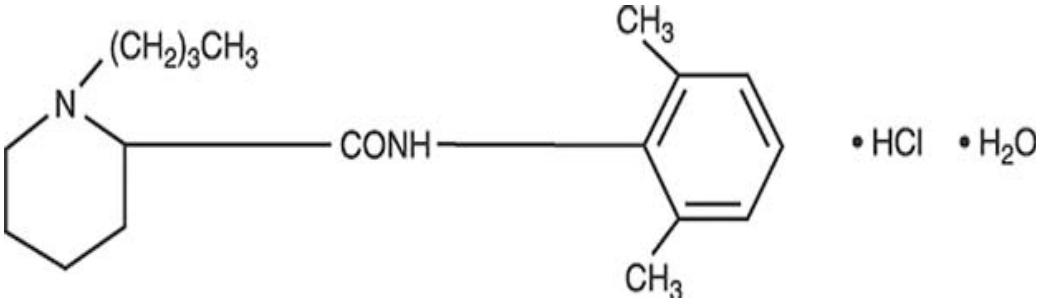
BUPIVACAINE HYDROCHLORIDE-

PHARMACOLOGY

Bupivacaine hydrochloride[4] is (±) -1-Butyl-2´,6´-pipecoloxylidide mono hydrochloride, mono hydrate. It is available as a white crystalline powder and in solutions. Powder form is freely soluble in 95% ethanol, water and slightly soluble in chloroform and acetone.

It is also available in Isotonic and hypertonic clear colourless solutions in varying concentrations.

STRUCTURAL FORMULA:



It contains an amide linkage between the aromatic nucleus and the amino or Piperidine group.

PHARMACOKINETICS

DISTRIBUTION:

After local administration, bupivacaine is absorbed systemically and distributed to all body tissues,especially to highly perfused organs like liver, lungs, heart and brain. It is also known to cross placenta.

The rate and degree of diffusion depends on:

a) Degree of lipid solubility (↑than lignocaine)

b) Degree of ionization (Pka = 8.1(↑than lignocaine)) and

c) Degree of plasma protein binding (↑than lignocaine).

pKa is 8.1. It is a weak base. The non ionised fraction at physiological pH(7.4) is 17%.

Onset of action : 20 – 30 mins

Duration of action: 3 to 5 hrs

Protein binding : >97%

T ½ :210 min

Toxic dose : 3mg/kg

Toxic serum level : >3ug/ml

METABOLISM:

Bupivacaine being an amide type local anaesthetic is metabolized mainly in liver by conjugation with glucuronic acid. So patients with severe hepatic disease are more prone to develop bupivacaine toxicity .Pipecolylxylidine is the larger inactive metabolite of bupivacaine.

EXCRETION:

Kidneys are the major excretory organ for bupivacaine. 6% of the unchanged drug is excreted by kidneys.

PHARMACODYNAMICS:

Systemic absorption of local anesthetics produces effects on CVS & CNS. At therapeutic doses,changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability and may lead to AV block, ventricular arrhythmias and cardiac arrest, sometimes death.

MECHANISM OF ACTION:

Bupivacaine produces conduction blockade by inhibiting the movement of sodium ions through ion selective Na+ channels in nerve membranes.K+ channels are also blocked.

Na+ channel permeability ↓

↓

Rate of depolarization ↓

↓

Threshold potential not reached

↓

Action potential not propagated.

Clinical use	**Concentration(in percentage)**	**Onset**	**Duration of action (in mins)**
Infiltration	0.25	Fast	120-480
Peripheralnerve block	0.25-0.5	Slow	240-960
Epidural	0.5-0.75	Moderate	120-300
Spinal	0.5-0.75	Fast	60-240

ADVERSE REACTIONS:

Cardiovascular manifestations of excessive plasma levels include myocardial depression, manifested as hypotension and cardiac arrest.

USES

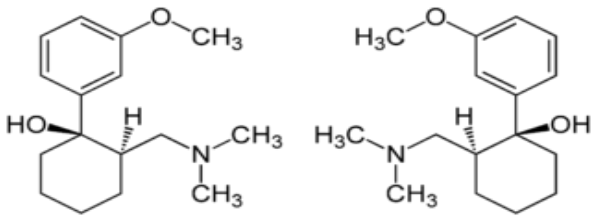
- Local Infiltration anaesthesia.
- Epidural Block
- Peripheral Nerve Block
- Central Neuraxial Blockade
- Patient Controlled Analgesia
- Labour Analgesia

PHARMACOLOGY OF TRAMADOL[5]

INTRODUCTION:

It is a weak opiod agonist. It is a synthetic analogue of codeine. It comes as racemose mixture. It was first introduced in year 1977.

STRUCTURAL FORMULA :



IUPAC NAME: 2-[(dimethylamino)methyl]- 1-(3-methoxyphenyl) cychexanol.

MECHANISM OF ACTION:

It acts on multiple receptors to produce analgesic effect. It is centrally acting . Tramadol acts on following receptors:

1. μ-opioid receptor agonist
2. serotonin releasing agent
3. norepinephrine reuptake inhibitor,
4. NMDA receptor antagonist

5. 5-HT_{2C} receptorantagonist

As a result of this naloxone does not fully affects its action. It produces less respiratory depression.

PHARMACOKINETICS:

Bioavailability is 68-74%, after oral dosing and 100% after intramuscular injection. Affinity for μ receptor is 1/6000 of morphine.

- It has 2 forms + and – enantiomers.
    - + enantiomer : μ receptor + serotonin uptake inhibition
    - -Enantiomer : nor epinephrine reuptake inhibition
- Tramadol comes as racemic mixture, thereby having synergistic effect
- Onset of action : 1 hr after oral dosing and 15-20 min after parenteral dosing.
- Peak plasma levels: 2- 3 hr
- Duration of action : 6 hr
- T ½ : 6 hr for tramadol.
- Metabolite O- desmethyl tramadol half life 7 and ½ hrs

PHARMACODYNAMICS

ABSORPTION:

It depends on mode of administration, dose and concentration.

Protein binding capacity is 20%

BIOTRANSFORMATION:

It is metabolised in liver by cytochrome enzymes CYP P450 isoenzyme. This involves CYP 2D6, CYP2B6, CYP3AP.

Metabolisation is affected by age and coexisting diseases. It is metabolised into O- desmethyl tramadol. This has 200 times more affinity towards u receptors. This prolongs duration of action.

EXCRETION:

After phase 2 metabolisation in liver water soluble metabolites are excreted by kidney.

USES:

Commercial preparations are available as capsules, tablets , extended release tabs, suppositories, parenteral preparation and topical gel/cream.

- Acute postoperative pain as an analgesic.
- As an adjuvant for spinal anaesthesia to prolong duration.
- As adjuvants and and also as sole agent in epidural block for pain relief.
- Post spinal shivering(DOC)
- Neuropathic pain.

ADVERSE EFFECTS:

- Nausea and vomiting (most common)
- Sedation , dizziness, headache
- Dry mouth, constipation
- Exacerbate seizures
- Itching
- Respiratory depression (minimal compared to other opioids)
- Physical and psychological dependance.

PARAVERTEBRAL BLOCK[6]

INTRODUCTION:

This involves use of local anaesthetic for providing anesthesia or analgesia for breast, thoracic and abdominal surgeries. This gives analgesia comparable to epidural with lesser side effects. Spinal nerves can be blocked at any level as they come out of intervertebral foramina. The paravertebral space contains spinal nerves, white and grey rami communicantes, the sympathetic chain, intercostal vessels, and fat .

ANATOMY:

It is triangular shaped and is present on either sides of vertebral column.

BOUNDARIES

SUPERIORLY : Superior Costotransverse Ligament (Extends Between Transverse Processes)

ANTEROLATERALLY : Parietal Pleura Of Lung

BASE : Posterolateral Part Of Vertebral Body, Intervertebral Foramen And Disc.

It Communicates With Ipsilateral Paravertebral Spaces Above & Below

LATERALLY – Intercostal Space

MEDIALLY – Via Intervertebral Foramen Into Epidural Space

Depending the site of surgery, corresponding nerves can be blocked. On the basis of nerves blocked paravertebral block can be divided into four types. They are:

- CERVICAL
- THORACIC (UPTO T 10)
- THORACO LUMBAR (UPTO L2)
- LUMBAR / PSOAS COMPARTMENT(UPTO L5)

It produces unilateral analgesia without much affecting the hemodynamic status.

In cervical and thoracic region only unilateral block must be done , to avoid bilateral phrenic nerve palsy or pneumothorax respectively. In lumbar regions bilateral block is possible.

INDICATIONS:

Postoperative pain relief using local anaesthetics and opioids

- Pain limited to particular dermatome
- Radicular pain due disc prolapse or intra and extradural spinal tumors
- Metastatic nerve invasion
- Rib fractures.

CONTRAINDICATIONS:

- Bilateral Cervical and thoracic blocks must be avoided in respiratory compromise
- Patients refusal
- Local sepsis
- Drug allergy

THORACIC PARAVERTEBRAL BLOCK[7]

Thoracic paravertebral blockade occurs on spinal nerves as they emerge from intervertebral foramen. After injection there is spread of drug to dermatomes above and below.

TECHNIQUE:

A thoracic paravertebral block can be performed with the patient in sitting ,lateral or prone position. The sitting position allows easy identification of landmarks. The thoracic spinous process of desired level is identified. After identification of spinous process ,with local infiltration by 1%lignocaine, 16 or 18 G TOUHY is introduced at 1.5 – 3cm lateral to spinous process and advanced in a direction perpendicular to the skin in all planes to contact the transverse process of the vertebra below. It is usually found at depth of 2 – 4 cm. Once the transverse process is identified, needle is redirected in a cephalad direction and gradually advanced till there is loss of resistance which corresponds to breech of costotransverse ligament. It usually occurs at 1 to 1.5 cm past superior edge of transverse process. If needle is directed caudally , chances of pneumothorax is less. After aspiration is found negative for blood the drug is injected. Other techniques include ultrasound guided and nerve stimulator guided blocks.

SPREAD OF DRUG INJECTED:

Drug spreads to paravertebral spaces above and below,laterally to Intercostal space , medially into epidural space and to contralateral paravertebral space. Usually spread limits to one Space above and below. A single dose of 15 ml causes unilateral blockade of 4 to 5 dermatomes. Spread of drug is more caudal then cephaloid. To achieve more intense blockade 4 to 5 ml of drug is injected in contiguous levels.

COMPLICATION:

Very rare possible complications include

- HYPOTENSION DUE TO SYMPATHETIC BLOCKADE.(4.6%)
- TOTAL SPINAL (0.1%)
- INTRAVASCULAR INJECTION(3.8%)
- PNEUMOTHORAX(0.5%)

UNIQUE FEATURES:

One of the most unique features of a thoracic paravertebral block is its ability to produce complete elimination of somatosensory evoked potentials. .They are eliminated at the block level and contiguous

dermatomes.Such an equivalent effect is not seen with any other type of neuraxial blockade.

Because of the effect of local anaesthetic drug action injected via the paravertebral space on the rami communicantes the quality of afferent blockade produced far exceeds that of spinal or epidural anaesthesia.Because of the propensity of the fibres to travel a certain number of dermatomes before reaching the spinal cord,central neural blocks do not afford complete analgesia.This explains the remarkable effect of paravertebral blocks to provide high quality analgesia in chronic pain syndromes.

ADVANTAGES OVER EPIDURAL BLOCKADE

Easier To Perform And Simple To Learn

Safety Profile Is Much Better

The incidence and magnitude of hypotension is significantly lower.

Unilateral blockade, less incidence of sympathetic block. .

.

OPIOIDS[8]

Opium is extracted from the capsule of poppy plants (Papaversomniferum). It is a brown residual material and has two active alkaloid ingredients, phenanthrenederiatives and benzoisoquinoline derivatives. Morphine, codeine and thebaine are derivatives of the former, while papaverine and noscapine are derivatives of the latter compound. Morphine is naturally available at 10% concentration in wild poppy.

CLASSIFICATION OF OPIOIDS:

Natural opioids: Morphine,Codeine

Semisynthetic opioids: Diacetylmorphine and Pholcodeine

Synthetic opioids: Pethidine, Fentanyl, Methadone, Dextropropoxyphene, Tramadol

GENERAL PHARMACOLOGICAL ACTIONS:

Analgesia:

Morphine is the most efficacious analgesic. The analgesia is dose dependent. Dull visceral pain is better relived than sharp somatic pain. The degree of analgesia is dose dependent. At high doses it can relieve even very

sharp somatic pain and to a very high degree. It is most efficacious at relieving nociceptive pain arising from stimulation of nerve endings compared to neuropathic pain arising from structural damage to nerve endings (ex. trigeminal neuralgia). In contrast to general anaesthetics, the suppression of pain sensation is selective and not dependent upon generalized suppression of all sensations and depression of the CNS.

Both perception of pain and the involved emotional concept(i.e the sensations associated with pain) are both altered. So pain is no longer perceived as an unpleasant sensation thereby increasing the threshold of tolerance. Intrathecal injection has been shown to cause segmental analgesia without affecting other modalities of sensation, while in the spinal cord it acts directly on the substansiagelatinosa to inhibit release of excitatory neurotransmitters from afferent pain neurons. This prevents the transmission of pain impulses. Specifically release of glutamate and its postsynaptic action on dorsal horn cells is prevented. Alteration of pain sensation happens due to action at the medulla, mid-brain and limbic and cortical areas. These together act to affect the way afferent pain impulses are processed and also generate feedback inhibitory impulses which are sent through the descending spinal pathways. Thus these spinal and supraspinal effects multiply to provide greater analgesia.

Sedation:

Indifference to self and surroundings accompanied by drowsiness occurs. This differs from hypnotics in that there is no motor incoordination involved. With increase in dose , sleep and coma can occur. In some people morphine and pethidine have been shown to precipitate epileptic seizures.

Mood and other subjective effects:

Opioids have a calming effect on the general population. There is loss of apprehension and a feeling of detachment. This detachment can even extend to self. There is a lack of initiative and mental clouding. All of these are perceived as unpleasant sensations in the absence of pain. But in the presence of pain or in addicts, these are perceived as welcome and pleasurable situations. The feeling of detachment is described as “floating” by addicts. A rapid i.v.injection of opioids give a rapid feeling of euphoria, termed as “High” or “Rush”. It is considered intensely pleasurable, not dissimilar to an orgasm. These effects are most likely mediated by dopaminergic neurons in the nucleus accumbens and the action of mu-receptors. A similar action on the kappa receptor in the same nucleus produces depletion of dopamine and produces an intense and opposite aversion. Also a similar action on locus cerulus produces fear and apprehension by blocking the release of nor-adrenaline.

Respiratory center:

The respiratory center gets depressed and both rate and tidal volume are affected. Multiple instances of death due to overdose have been recorded. In addition to depression of the respiratory center, there is indifference to breathing by the apneic patients themselves. They may not breath unless commanded to do so.

Cough center:

The cough center is affected more than the respiratory center. Cough reflex is suppressed severely even at low doses. This is being used in cough suppressants like codeine.

Neuroendocrine system:

Hypothalamic afferent collaterals are suppressed. There is universal suppression of all neuro-endocrine secretion. The posterior pituitary is affected more than the anterior pituitary. But these effects are short-lived and tolerance develops to these effects immediately.

Cardio-vascular system:

Morphine causes differential vasodilation which is greater in the systemic circuits compared to the pulmonary circuits resulting in a shift of

blood to the systemic circulation. The vasodilation is mediated by multiple mechanisms including release of histamine, a direct depressant action on the vasomotor center and a direct action on the tone of the vessels. This results in overall reduced cardiac output due to the decreased peripheral resistance.

GIT:

Constipation is a major result of the action of morphine. There is increased tone and segmentation movements but decreased propulsive movements. Spasm of pyloric and ileocaecal and anal sphincters can occur. Also there is a central action causing inattention to defecation reflex.

Other smooth muscles:

Morphine causes spasm of the sphincter of Oddi. This can result in increased biliary pressure and biliary colic. This action is partially relieved by atropine and completely by the opioid antagonist naloxone. The tone of both detrusor and the sphincter is increased resulting in difficulty in micturition and a feeling of urgency. It may slightly prolong labor and cause significant bronchoconstriction in asthmatics due to the release of histamine.

Pharmacokinetics:

A high and variable first-pass metabolism results in poor oral absorption of morphine with only about 20-25% bioavailability. There is a

very high amount of distribution in the tissues compared to the plasma resulting in a high volume of distribution. The half-life of the drug ranges from 4-6 hours because of the extensive tissue distribution.

Adverse Effects:

Dysphoric effects like sedation, lethargy and clouding of cognition can happen in a number of people. Unless they are addicts these effects are mostly perceived as unpleasant. Vomiting, constipation and respiratory depression are common and expected at even low therapeutic doses. Blurring of vision and urinary retention can happen in the elderly. Some fall in BP can occur in mobile patients. Allergic reactions have been reported but are few and far between. Local reactions at the sites of injections are more common (Histamine release). Morphine can cross the blood-placental barrier and cause aponea in the newborn if given to the mother. This is easily reversed by injecting naloxone (through the umbilical chord).

Dependence and Tolerance:

Morphine exhibits a high degree of tolerance. People become tolerant even after a single dose of morphine. The tolerance is explained partly by the increased metabolism and the consequent increase in elimination. But most of it is due to the increased cellular tolerance. Tolerance occurs for all

actions except constipation and miotic effects. Also subjects tolerant to morphine exhibit tolerance to most CNS depressants as well.

Morphine produces physical and psychological dependence probably through NMDA and Nitric Oxide dependent mechanisms which are probably the same mechanisms involved producing in the analgesic effect of the drug. Now, usage of morphine has been curtailed by the medical community because of its abuse potential. But studies show that valid medical use of morphine has rarely lead to the dependence in patients.

Withdrawal leads to drug seeking behavior in patients. Physical manifestations seen are mostly the opposite of the effects – lacrimation, sweating, diarrhea, mydriasis, hyperventilation, vasoconstriction and if prolonged weight loss and suicidal tendencies. These effects are precipitated in animal model s and humans by injection of pure opioid antagonists.

Interactions:

Tricyclic anti-depressants, Mono-amine oxidase, phenothiazine, amphetamines and neostigmine potentiate the effect of morphine. Morphine in turn retards the digestion of drugs by delaying gastic emptying.

POST OPERATIVE NAUSEA AND VOMITTING

INTRODUCTION:

Post operative nausea and vomiting is defined as nausea and/or vomiting occurring within 24 hrs after surgical procedure. 20 – 30% of normal persons and 70-80% of high risk patients are affected by PONV.

RISK FACTORS:

Four major risk factors associated with post-operative nausea and vomiting are:

a) Females

b) Non-smoker

c) History of motion sickness

d) Use of post-operative opioids.

ETIOLOGY:

Etiology of PONV is multifactorial as Individual, anaesthetic and surgical risk factors are involved.

Individual factors:

Females have increased risk of PONV than males but the reason for increased susceptibility is still unclear. Smokers are desensitized to nausea due to their previous exposure to nausea and vomiting during smoking.

Previous H/OMotion sickness

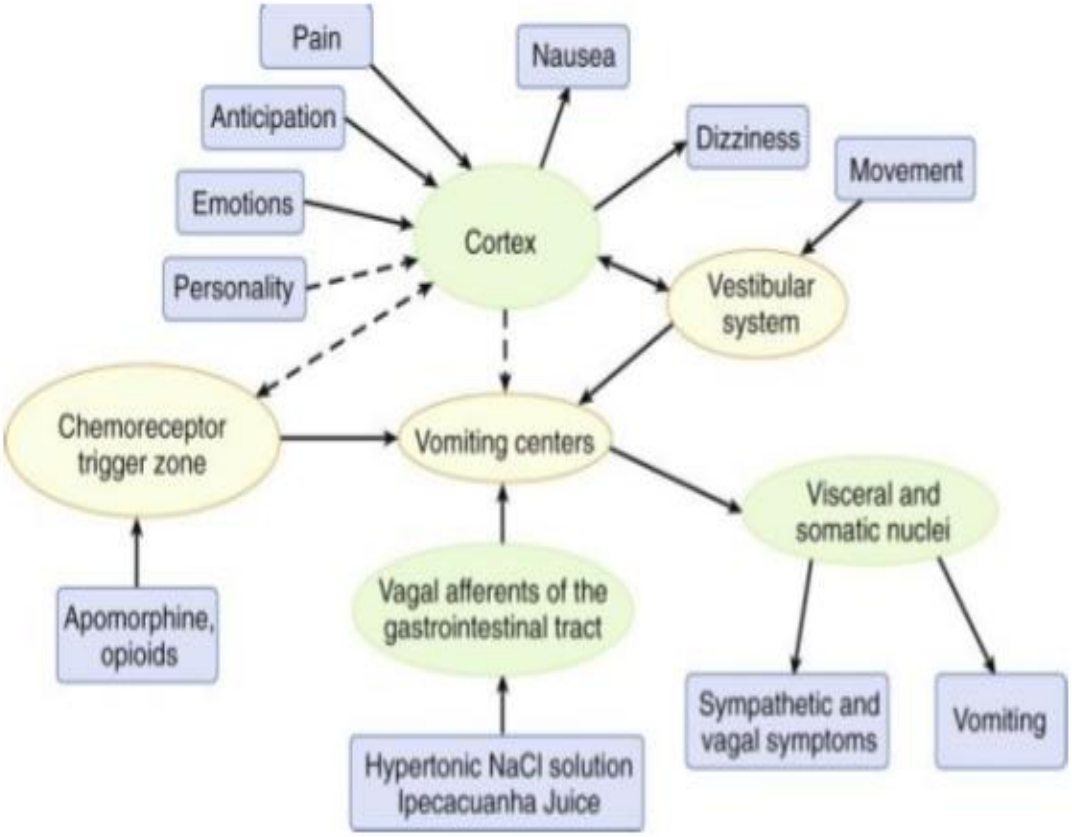
Age has shown to reduce the incidence of Postoperative nausea and vomiting but it is not a strong risk factor.

Anaesthetic factors:

Usage of volatile anaesthetics, Nitrous oxide,opiods and high dose of neostigmine (2.5mgs) leads to increased incidence of Postoperative nausea and vomiting.

Surgical factors:

Thirty minutes increase in duration of surgery increases the risk of PONV by 60%.



RECEPTORS INVOLVED IN PONV:

a) Serotonergic receptors

b) Dopaminergic receptors

c) Histaminergic receptors

d) Cholinergic(Muscarinic) receptors.

METHODS TO REDUCE PONV IN PERIOPERATIVE PERIOD

- Administer regional anaesthesia whenever possible than General anaesthesia because General anaesthesia is associated with 11 times increased incidence in post opeative nausea and vomiting.

- Supplemental oxygen peri-operatively has been shown to reduce the Postoperative nausea and vomiting by 50%.

- Intra venous fluids have shown to reduce the incidence of PONV by the mechanism as it prevents the release of serotonin in GI tract due to GI hypoperfusion as caused by the induction agents.

- Treatment with NSAIDS instead of opioids in the intra operative and postoperative period have shown to reduce the incidence of postoperative nausea and vomiting.Usage of post-operative opioids doubles the risk of Postoperative nausea and vomiting.

- Whenever General anaesthesia is required the use of Propofol as the induction agent reduces the early incidence of PONV as compared to other induction agents. Using propofol in patient

controlled anaesthesia in plasma concentrations of 343 ng/ml has shown to reduce the incidence of PONV by 50%. Neostigmine which is a reversal agent for non-depolarizing muscle relaxation is associated with increasesd incidence of PONV when used in high doses ,especially greater than 2.5mgs,and should be avoided if possible.

AIM OF THE STUDY

To Study The Effectiveness Of Thoracic Paravertebral Block Versus Systemic Opioids For Relief Of Post Operative Pain In Patients Undergoing Mastectomy Under General Anaesthesia.

MATERIALS AND METHODS

This study was conceived and designed as a prospective, randomized study. We performed this study after getting institutional ethical committee approval (Government Kilpauk Medical College). This study was performed in adult women aged 18-60 years with Body mass index from 18.8 -24.0 belonging to American Society of Anaesthesiolo gists ASA 1and2 undergoing elective modified radical mastectomy under general anaesthesia. Cases were mainly done in the general surgery and oncology department of this institute.

Group A :

Twenty five patients receiving standardized general anaesthesia for surgery with thoracic paravertebral block (0.3 ml / kg or 1.5 mg / kg of 0.25%. Bupivacaine at levels T3 and T5).

Group B :

Twenty five patients receiving standardized general anesthesia for surgery with systemic opioids. All patients received injection tramadol 100 mg intravenously for post operative pain relief.

The procedures were thoroughly explained to the patient and informed written consent was obtained. Basic anthropometric data like age, height, BMI, ASA class, etc were clearly noted down. Baseline investigations were checked. Airway assessment was done methodically on each and every patient and history of comorbid illness elicited. The patients were assessed for GA under ASA I and II with the following inclusion and exclusion criteria.

INCLUSION CRITERIA:

ASA 1 to 2

18 to 60 years

Female sex

Elective modified radical mastectomy

Undergoing general anaesthesia .

EXCLUSION CRITERIA :

Cellulitis or infection at the site of needle puncture .

Coagulation disorders

Cardiac problems

Renal failure

Neurological and mental illness

Deformity of spinal column

Previous thoracotomy

Allergic to local anaesthetics

PREOPERATIVE ADVICE:

A fasting period of eight hours was advocated as a minimum. A 16 G Intravenous cannula was inserted on the appropriate side. All patients receive an antacid prophylaxis of injection ranitidine 50 mg IV. All the patients are premedicated with injection glycopyrrolate 0.2 mg IM one hour before surgery.

In the preoperative patient waiting room, the following baseline parameters are noted

1. Pulse rate

2. Systolic blood pressure

3. Diastolic blood pressure

4. Mean Arterial pressure

5. Respiratory rate

MONITORING :

INTRAOPERATIVE

- Pulse Oximetry
- Non Invasive Blood Pressure.
- ECG
- End Tidal Carbon Di Oxide Analysis.
- Temperature

Conduct of General anaesthesia

- After shifting the patients to operation theatre patients are connected to ECG, pulse oximetry, NIBP, and EtCO2 monitors.
- All patients are started with ringer lactate at 100 ml/hr.
- All patients are given fentanyl 2µg/kg IV and pre oxygenated with 100% oxygen for 3 – 5 minutes.

- The trachea was intubated after induction of anaesthesia with propofol 2 mg / kg and atracurium 0.5 mg/kg.

- Anaesthesia was maintained with 1-1.5% sevoflurane and 2 litres of nitrous oxide and 1 litre of oxygen.

- At the end of the surgery patients in group A (study group) turned to lateral position and a thoracic paravertebral block with 0.25% bupivacaine 0.3 ml/kg or 1.5 mg / kg given at levels T3 and T5.

- When Patients had spontaneous respiratory attempts they were reversed with neostigmine 50 mcg/kg and glycopyrrolate 20 mcg/kg.

- Numerical pain scale were recorded 20 min after giving block or extubation which ever is latter.

- Patients in group B(control group) were extubated using standard extubation criteria. 100 mg of tramadol was given intravenously twenty minutes before extubation in group B.

TECHNIQUE OF PARAVERTEBRAL BLOCK

In group A under strict aseptic precautions, after local infiltration with 2 ml of 2% lignocaine a18 G epidural needle was introduced through the skin, approximately 3 cm lateral to the midline on the side of surgery and the level corresponding with the cephalad end of the spinous process. The needle was then advanced 90 degrees to the skin, till it contacted the transverse process. The needle was then walked over the top of the transverse process. At this point, the L.O.R. syringe was attached to the epidural needle and further advancements of the needle was done in small increments. Loss of resistance was used to identify the paravertebral space. Injections were given in two spaces of T_3 and T_5 to achieve block from T_3 to T_8 which is normally required for mastectomy.

Since the block is performed at the end of the procedure all the patients both study and control group were kept in the post anaesthetic intensive care unit for the first 24 hours and closely monitored.

POSTOPERATIVE MONITORS:

- Noninvasive Blood Pressure
- Pulse rate

- Oxygen saturation
- Numerical pain scale

Vital parameters (pulse rate, systolic and diastolic blood pressure and respiratory rate) and VAS score were compared between two groups at every10 min upto one hour, and then every 30 min till 6 hours.

The time tested visual analogue scale was demonstrated to the patients. On a 10 cm long scale, they were told that 0 represented “no pain” and ten worst” considerable pain”.

Post operatively the following parameters were noted and taken for statistical analysis.

1. Tine duration of complete analgesia
2. Duration of effective analgesia
3. Hemodynamic stability
4. PONV incidence
5. Sedation
6. Type of rescue analgesia and time

7. Incidence of pneumothorax by checking air entry/X-RAY.

RESCUE ANALGESIA

Rescue analgesia were given with inj diclofenac 75 mg intramuscularly in both the groups.

Procedure was considered as a failure:

In group A (study group), at the first assessment which was done at 30 minutes after thoracic paravertebral block with 0.25%. Bupivacaine, if the pain relief was not satisfactory. .

POST OPERATIVE SIDE EFFECTS :

- Hypotension was defined as fall in mean blood pressure to more than 20% its baseline value. It was managed with iv. fluids and with incremental doses of Inj. Ephedrine 6 mg.

- Bradycardia was defined as fall in heart rate <55 / min and was managed with Inj. Atropine 0.6 mg.

- Incidence of PONV (postoperative nausea and vomiting) was studied in both groups and Inj. Ondansetron 0.1 mg/kg intravenously was given to manage it.

- The need for rescue analgesia (Inj. diclofenac) was noted in both the groups
- Hemodynamic parameters were studied in both the groups and compared
- Other side effects monitored were
    - Pruritis
    - Allergic reactions
    - Respiratory depression
    - pneumothorax

REVIEW OF LITERATURE

Pain has now been designated as the fifth vital sign and its regular monitoring has been advocated. A good regimen for postoperative analgesia has multifold beneficial effects for the patient.

1. The recovery after surgery is smooth and recovery time is significantly shortened.

2. The detrimental effects of postoperative inflammatory mediators induced by surgical stress is significantly reduced.

3. Respiratory function is much improved in terms of spirometry valuesand patient comfort is better.

4. It helps to maintain hemodynamic stability and reduces the stress response.

There are a lot of studies that have evaluated the efficacy of thoracic paravertebral block in reducing the complications of postoperative pain in a variety of surgical procedures like thoracotomy, mastectomy, cholecystectomy. I have presented here certain relevant review of literature.

1. **S.M. KLEIN**[9] et al did a single blind, prospective randomized study of 60 women posted for unilateral breast augmentation surgery. Patients were randomly allocated (n = 30) to receive a general anaesthetic (GA) or thoracic paravertebral. Block. The study used visual analog scale score and postoperative –nausea and vomiting scores. The study found out that VAS score was statistically significantly lower in the paravertebral group at 30 min (p = 0.005), 1 hour (p = 0.0001) and 24 hr (p = 0.04). The incidence of PONV in the paravertebral block group at 24 hour (p = 0.04) was also significantly lower. However, no statistical significance was found out in PONV at 30 min or 1 hr.

The study concluded that paravertebral block in conjunction with general anaesthesia provides pain relief with fewer side effects, than conventional standard general anaesthesia.

2. **TAHIRI. Y**[10] et al did a meta analysis with data collected from the year 1980 until the end of June 2010. They used a computerised database collection of articles comparing thoracic paravertebral block with general anaesthesia (GA) in patients who underwent breast surgery. Meta analysis was studied using mantel – Haenzel method.

In the eleven studies used for analysis, pain scores were significantly reduced at 1 and 6 hr postoperatively in the paravertebral block group as

compared to GA (mean difference of 2.48) and 1.71 Also, the consumption of postoperative analgesics was found to be significantly lower in patients on TPVB than GA (Relative Risk 0.23). The incidence of PONV (RR 0.27) with 95% confidence interval was again significantly lower in PVB group than GA.

The study concluded that paravertebral block group results in significant benefits to the patient for ambulatory breast surgeries when compared to GA alone. However, they advised ultrasound guided blocks to improve the safety of the procedure.

3. **Ono. K and koyama T**[11] et alundertook a study comparing the combined use of Thoracic paravertebral block with general anaesthesia for major breast surgery compared with GA alone. surgical anaesthesia with TPVB alone causes considerable discomfort to the patient. In this prospective, randomized, trial, 28 patients of (ASA I – III) class who underwent modified radical mastectomy were given TPVB as a single shot injection with 15 ml of 0.5% ropivacaine. This was done before induction of general anaesthesia.

The parameters that were observed in the postoperative period were

1. Visual analogue scale score

2. Consumption of postoperative analgesics.

This was compared with a standardized general anaesthetic alone.

Analgesia as evaluated by the VAS scores in the TPVB group were 34 +/- 4 ½ MIN in the post anaesthesia care unit and 15 +/-5 min next morning consumption of postoperative analgesics was significantly less in the TPVB group.

4. **TAREKH** M.A[12]. shams et al did a prospective, randomized, double blind study to compare the effectiveness of TPVB for relief of postoperative pain in breast cancer patients compared to intrapleural analgesia. They randomized patients into two groups. group a receiving TPVB and Group B receiving intrapleural analgesia. The following parameters were studied.

1. Duration of analgesia

2. Patient comfort was studied using "PRINCE HENRY" Scale or verbal rating scale.

3. Hemodynamic parameters

4. Postoperative nausea and vomiting.

They concluded that Group A (ii) thoracic paravertebral group patients had significantly better patient comfort, better hemodynamic stability and also the incidence of PONV was significantly lower.

5. **Parul Bansal**[13] et al did a study to evaluate the efficacy of thoracic paravertebral block with wound infiltration of 0.5/- (H) Bupivacaine in patients undergoing modified radical mastectomy. It was a prospective, randomized double blind study for which forty patients enrolled. Two groups were divided.

- 0.3 ml / kg of 0.25% (H) bupivacaine by continuous paravertebral infusion.
- 0.3 ml / kg of local wound infiltration

Statistical analysis were performed using unpaired student 't' test. They concluded the following

1. In the paraverterbral group, VAS scores were significantly lower than the wound infiltration group at any point of time in the first 24 hours.
2. Not even a single patient in the paravertebral block group required tramadol whereas the mean requirement of tramadol in wound infiltration group was -10 $\pm$ 2 mg / kg.

3. PONV scores were significantly better in the TPVB group.

6. **Jerzy paleczcy'**[14] et al did a double blind, prospective, randomized study to crystallize the effects of general anaesthesia with unilateral paravertebral block for open cholecystectomy. After obtaining ethical committee approval, 60 patients were randomized into two groups. Group A (n = 20) received standardized general anaesthesia, while group b (n = 20) received TPVB along with general anaesthesia. The parameters studied were

1. Hemodynamic stability

2. Frequency of PONV

3. Pain using the VAS score

They found out that during the first three days after surgery, Group b patients had significantly lower VAS scores ($p < 0.005$) PONV was significantly higher in Group A (60% V 33%) ($p = 0.0007$).

They concluded that the combination of TPVB along with GA significantly improved the patient comfort and reduced the side effects associated with GA alone.

7. **Pasch p. Acta** did a prospective, randomized double blind clinical trial comparing the efficacy of multiple level single shot thoracic paravertebral block with standardized general anaesthesia to patients (ASA Class I & II). They concluded the following.

1. VAS scores in the thoracic paravertebral block group were significantly lower ($p < 0.05$).

2. The incidence of pain and restriction of movements was also significantly lower ($1 < 0.0001$).

3. The incidence of PONV ($p > 0.05$) was lower

4. Shorter duration of hospital stay

8. **Gamal Z**[15] et al did a study to compare the efficacy and limitations of thoracic epidural with thoracic paravertebral block in paediatric cardiac surgery. Theirs was a prospective, randomized, double blind study on 60 paediatric patients scheduled for thoracic procedures under AS A II – III.

Group A was the thoracic paravertebral group and Group B was the thoracic epidural. The following parameters were studied.

1. VAS score for the first 24 hours (hourly monitoring)

2. Plasma cortisol 8th hourly assays

3. Spirometry 6 hours postoperatively

They concluded that postoperative pain relief, serum cortisol level, and spirometry values were comparable. However, the incidence of hypotension and PONV were significantly lower in TPVB then epidural.

9. **Azad**[16] et al in his study compared patient controlled analgesia systems (using an intravenous drug) piritramid, versus continous thoracic paravertebral block infusion (Bupivacine 0.125%). They did a prospective double blind randomized study for which 50 patients enrolled. The paravertebral infusion consisted of 0.125% Bupivacaine + fentanyl 5 mg / ml at a flow rate adjusted from 4-10 ml / hr.

In the pc 4 group, 25 patients received intravenous piritramid (Bolus 2, 5 mg, lock out 15 minutes).

- Visual analogue scale scoring found out that VAS scores were significantly lower in the paravertebral group. spirometry values and a lower incidence of PONV were also reported Hospital stay was also shortened. No major complications were observed in either group.

The conclusion of the study was that paravertebral infusion with local anaesthetic and fentanyl provided better comfort and a lower incidence of PONV relative to intravenous PCA.

10. **Joshi**[17] et al evaluated a meta analysis of studies evaluating the efficacy of various regional techniques. Thoracic epidural, Thoracic paravetebral block, Intrathecal, and interpleural analgesic techniques were compared with one another and also to systemic opiods.

The parameters studied were

1. Postoperative pain using the visual analogue scale
2. Consumption of opioids
3. PONV

- The study concluded that among the various regional techniques, paravertebral block infusion was equipotent to epidural block, albeit with a lower incidence of hypotension. Also, paravertebral block decreased the incidence of PONV and pulmonary complications. Also All of the regional techniques were superior to systemic opioids.

11. **Davies**[18] et al using statistical studies conducted a meta analysis of a large number of prospective, randomized trials comparing thoracic paravertebral block, Epidural block and systemic opioids. No statistical significance was found out between, TPVB and epidural with regard to pain at the first or second day. However, PONV and the incidence of pulmonary complications were significantly lower in TPVB. Also, PONV & Higher

VAS scores were documented in the opioid group. Rate of failure was significantly lower in the PVB group.

The conclusion was that TPVB was much superior to systemic opioids with regard to patient comfort and decreased complications.

12. **Santhosh** et al did a prospective, randomized, double blind comparing TPVB and TEA. Dividing the group of fifty into twenty five each, they were randomized to receive 8 ml of 0.25% Bupivacaine either in the thoracic paravetebral region or the thoracic epidural region at the conclusion of the surgery.

VAS scores were comparable in both the groups at 24 and 48 hours. However, the incidence of hypotension is significantly higher in the epidural block than TPVB. Also, the failure rate was higher in TEA than TPVB.

The study concluded that even though TEA and TPVB are comparable as far as postoperative analgesia is concerned, the failure rate and complications are much lower in TPVB.

TPVB – Thoracic paravertebral block

TEA – Thoracic epidural anaesthesia

13. **Sabyascachi Das**[19] et al did a prospective, randomized trial comparing the efficacy of unilateral thoracic PVB with standardized general anaesthesia. In this, patients belonging to age group 18-65 years, of ASA (status I – II) posted for unilateral mastectomy were randomized into group p (n 30), TPVB or group G (n-30) GA.

- They concluded that the duration to first postoperative analgesia was significantly higher in TPVB than GA p (304 min) VSG (132 min). $p > 0.001$. The consumption of postoperative analgesics and the need for rescue analgesia was significantly higher in standardized general anaesthesia. PONV requiring treatment was significantly higher in GA than TPVB. The conclusion was that TPVB was more efficacious than standardized general anaesthesia in unilateral breast surgeries.

14. **Preethy J. Mathew**[20] et al did a randomized clinical study to evaluate whether a lower concentration of bupivacaine had a similar efficacy and lower Toxicity profile when compared with higher concentration (0.5%) bupivacaine. In this study, forty eight patients took part. They were put into one of four groups.

Group 1 : 0.25% Bupivacaine + 5 μg/ml epinephrine

Group 2 : 0.25% bupivacaine + 5 μg/ml epinephrine

+ 2 μg/ml fentanyl

Group 3 : 0.5% Bupivacaine + 5 μg/ml epinephrine

Group 4 : Isotonic saline

A dose of 0.3 ml / kg of the test solution was injected in the paravertebral space. This was done before induction of the patient. They concluded that lower concentrations of Bupivacaine had the same efficacy, at the same time the toxicity profile was significantly lower.

OBSERVATION AND RESULTS

Our study was a prospective , randomized study to compare the hemodynamic stability ,postoperative analgesia using the visual analogue scale scoring system and the incidence of postoperative nausea and vomiting of thoracic paravertebral block and systemic opioids in randomly selected adult women undergoing modified radical mastectomy under general anaesthesia.A total of Fifty patients were taken into the study out of which 25 belonged to study group A(thoracic paravertebral block with 0.25% bupivacaine and the other 25 patients to control group B(Systemic opioids) who received injection tramadol 100 mg intravenously 20 mins before extubation.

The statistical analysis of the observed parameters for the study was done using SPSS for windows version 15.0.The results of the study were expressed in terms of mean and standard deviation.The quantitative aspects of the study was computed by using the t-test.The qualitative aspects of the study were compared using the chi-squared test or fischer's exact test.Results are displayed in bar charts and appropriate diagrams.

A p value of less than 0.05 was taken as statistically significant.The results of our study are published below.

Demographic profile of Age

Group	Number of patients	Mean	Std. Deviation	P-value
Group_A	25	40.92	4.754	0.787
Group_B	25	41.32	5.588	

The mean age of group A was 40.92 and group B was 41.32.There was no significant (P=0.787) difference between the mean age of these two groups ,which implies both groups were similar with respect to age.

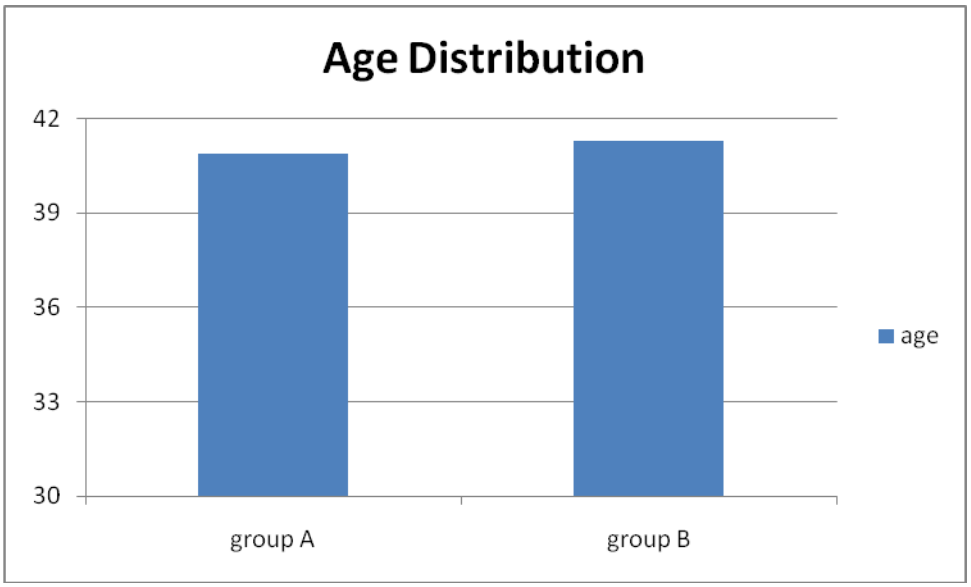


Table-1

Demographic profile of BMI

Group	Number of patients	Mean	Std. Deviation	P-value
Group_A	25	20.9	1.61	0.636
Group_B	25	20.8	1.56	

The mean BMI of group A was 20.9 and group B was 20.8.There was no significant (P=0.636) difference between the mean BMI of these two groups ,which implies both groups were similar.

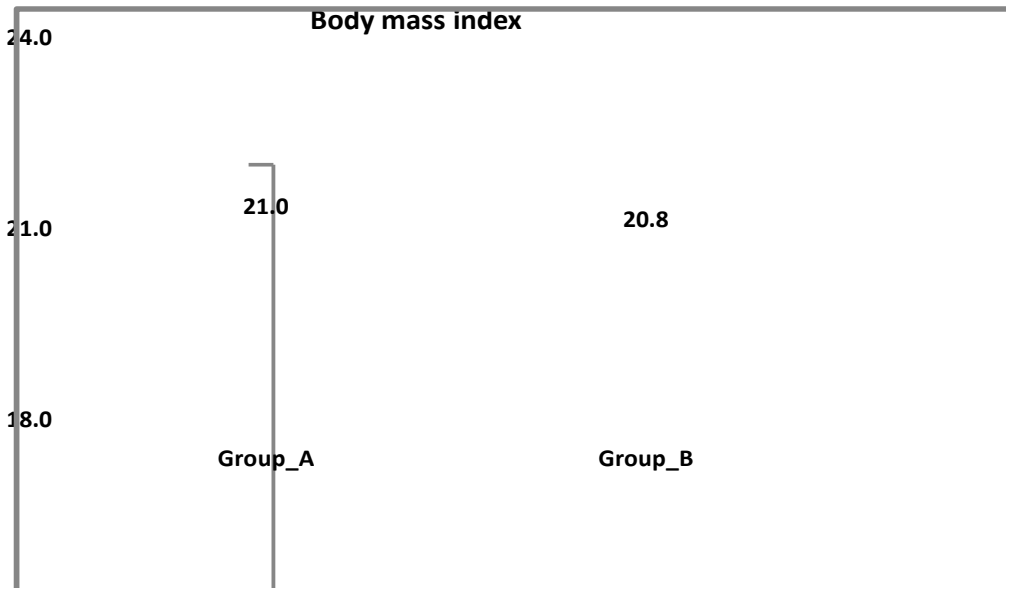


Table-2

Time to reach complete Analgesia

Group	Number of patients	Mean	Std. Deviation	P-value
Group_A	25	43.79	7.193	0.000
Group_B	25	31.16	6.108	

In group A the mean time to reachcomplete analgesia was 43.79 minutes and in group B was 31.16. The mean time to reach complete analgesia in group B is significantly ($p<0.05$) lower compared to group A

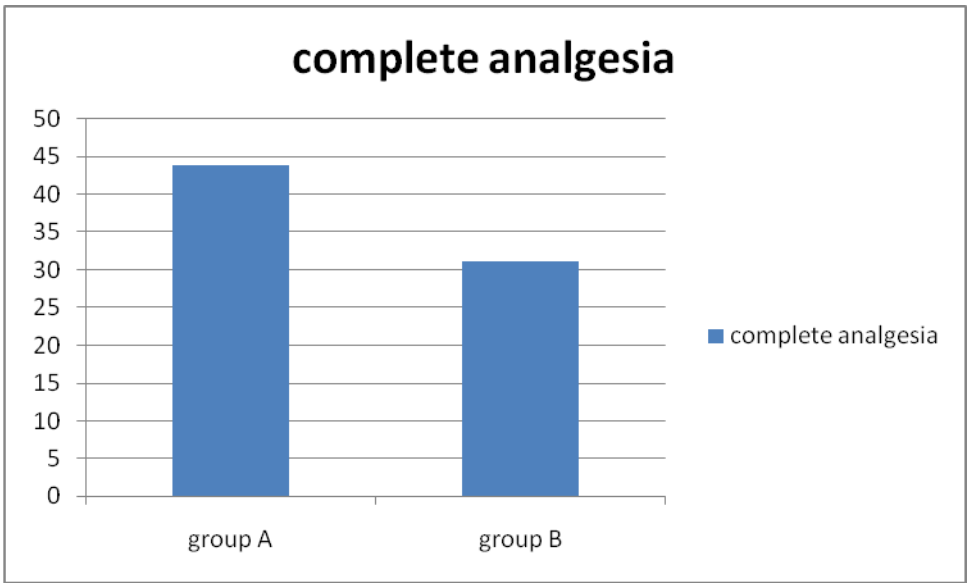


Table 3

Time duration of effective Analgesia

Group	Number of patients	Mean	Std. Deviation	P-value
Group_A	25	308.71	28.764	0.000
Group_B	25	144.24	20.648	

In group A the mean time of effective analgesia was 308.71 minutes and in group B was 144.26. The mean time of effective analgesia in group A is significantly ($p<0.05$) higher compared to group B.

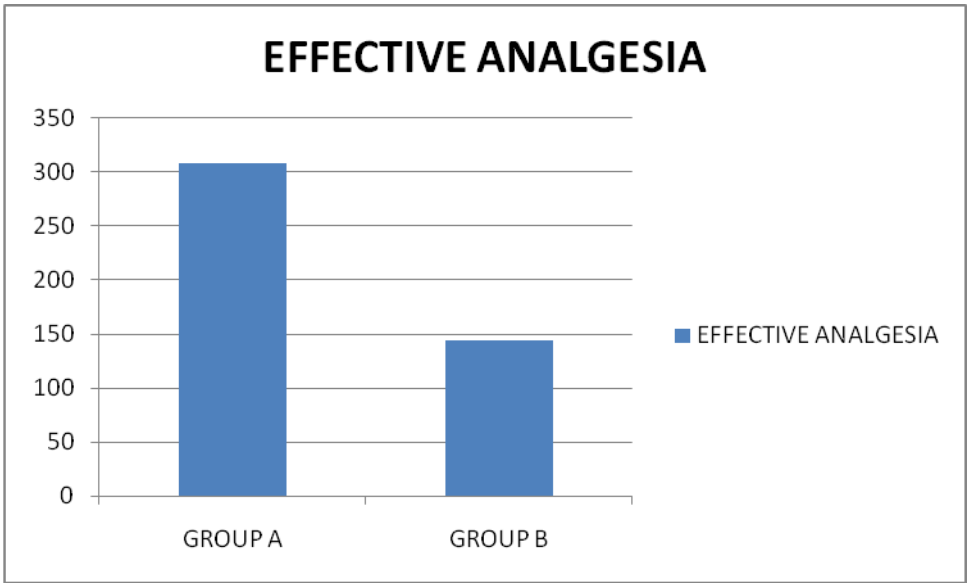


Table-4

Pulse rate changes in the post operative period in both groups

Minutes	Group	Pulse rate Mean	Std. Deviation	P-value
baseline	A	81.29	5.729	0.630 NS
	B	80.40	7.042	
10	A	83.67	6.225	0.001 S
	B	93.64	12.786	
20	A	86.17	6.211	0.001 S
	B	96.60	13.342	
30	A	85.88	6.550	0.001 S
	B	95.76	12.444	
40	A	83.79	6.164	0.000 S
	B	97.00	13.401	
50	A	82.62	6.749	0.000 S
	B	95.32	12.075	
60	A	82.46	6.108	0.000 S
	B	95.16	12.999	
90	A	84.92	5.664	0.004 S
	B	92.80	11.427	
120	A	87.33	5.654	0.002 S
	B	96.32	11.803	
150	A	90.67	6.592	0.213 NS
	B	94.20	12.083	
180	A	91.33	7.998	0.463 NS
	B	93.52	12.163	
240	A	87.29	7.298	0.028 S
	B	93.88	12.350	
300	A	83.54	6.587	0.001 S
	B	94.68	13.322	
360	A	83.96	6.817	0.000 S
	B	94.92	11.913	

At base line the mean pulse rate (per/minute) there is no significant(P>0.05) difference between the groups. But the significant (P>0.05)difference is observed from time point 10 minutes to 120 minutes, later on from 150 minutes to 180 it is found there is no significant difference (p>0.05). It is also observed again significant difference of mean pulse rate between the groups from Four hours to six hours.

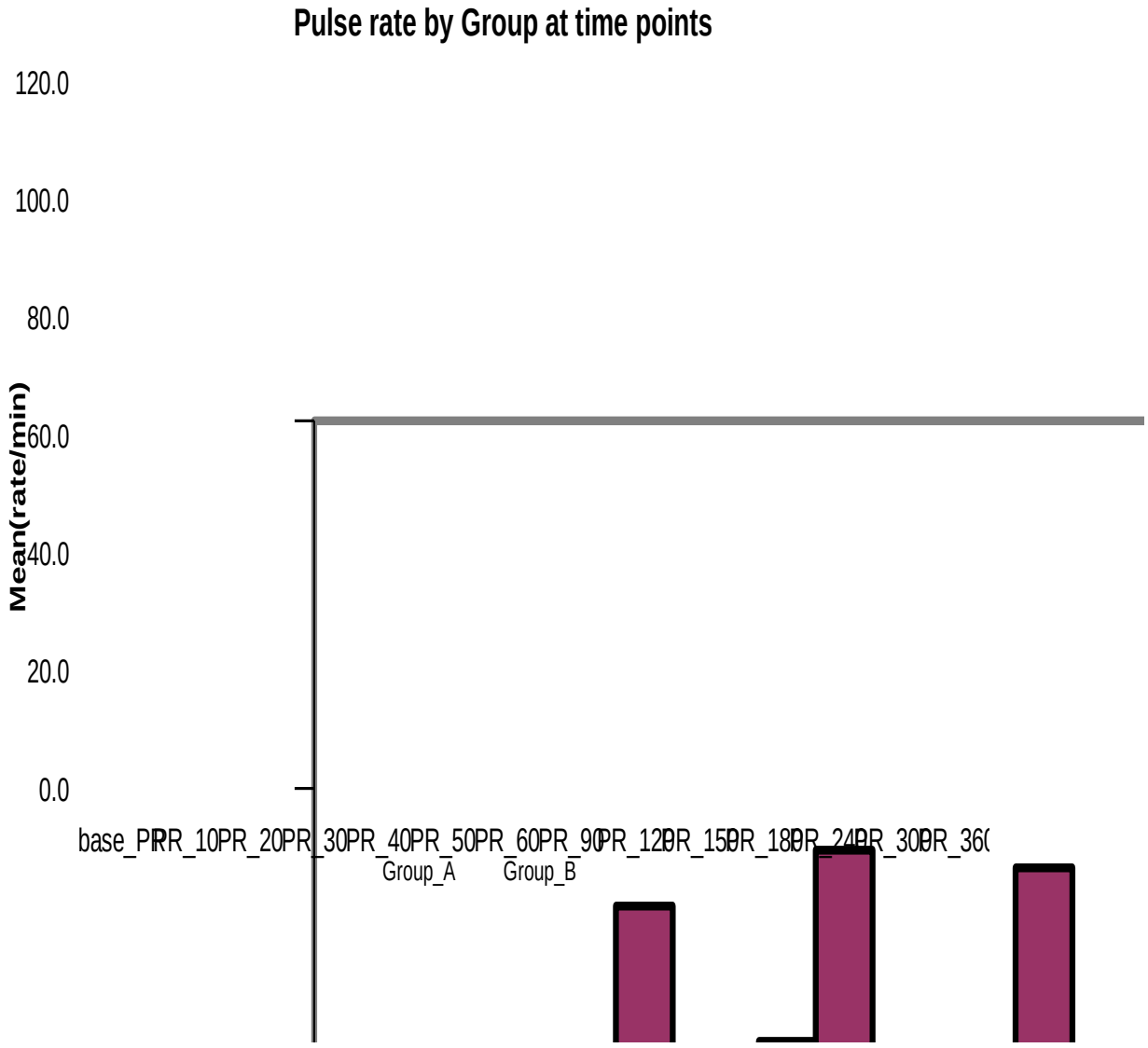


Table-5

Systolic blood pressure changes in the postoperative period by groups at different time points

MINS	Group	Systolic BPMean	Std. Deviation	P-value
Baseline	A	121.83	9.563	0.998
	B	121.84	8.425	NS
10	A	120.33	10.909	0.027
	B	128.04	12.595	S
20	A	110.25	9.128	0.000
	B	126.56	14.373	S
30	A	109.92	10.363	0.003
	B	121.96	15.773	S
40	A	108.58	8.209	0.000
	B	121.92	14.517	S
50	A	111.92	9.399	0.000
	B	126.04	13.612	S
60	A	114.12	8.425	0.000
	B	128.52	13.821	S
90	A	117.58	8.032	0.003
	B	128.52	14.984	S
120	A	119.21	7.593	0.003
	B	129.08	13.653	S
150	A	120.92	8.081	0.002
	B	129.68	10.723	S
180	A	121.54	6.821	0.001
	B	130.48	10.642	S
240	A	121.00	7.896	0.012
	B	129.08	13.099	S
300	A	120.58	6.865	0.000
	B	130.92	11.053	S
360	A	121.83	9.145	0.001
	B	131.40	9.929	S

At base line the mean systolic blood pressure (mm/Hg) it is observed there is no significant(P>0.05) difference between the groups. But the significant (P>0.05)difference is observed between the groups at all time points i.e10 minutes to 360 minutes. Also it is noticed that in all the time points the mean SBP is significantly higher in group B (control)compared to group A(study)

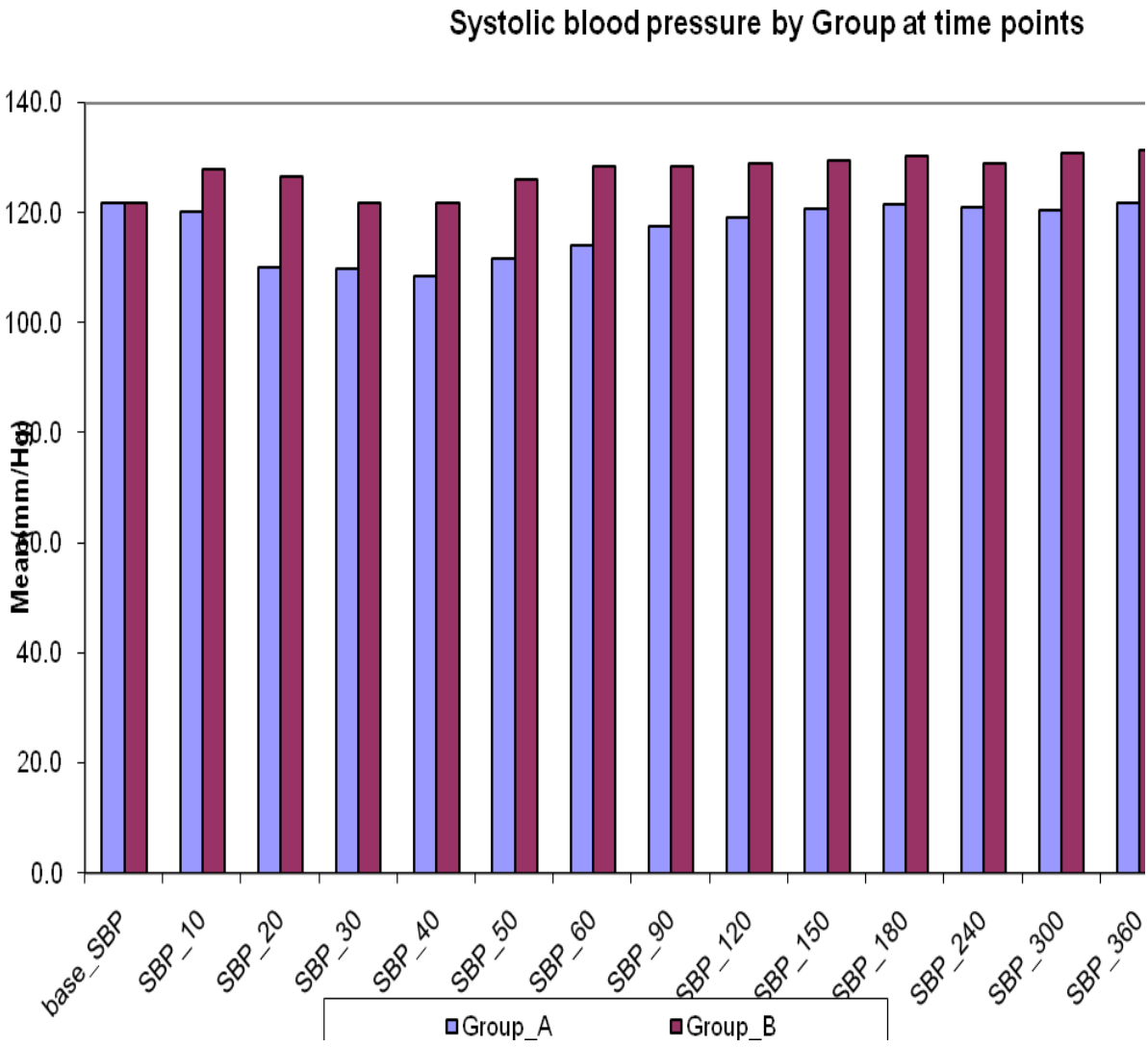


Table -6

Diastolic blood pressure changes in the postoperative period by groups

MINS	Group	DiastolicbpMean	Std. Deviation	P-value
Baseline	A	80.58	8.392	0.378
	B	78.44	8.476	NS
10	A	78.83	7.938	0.001
	B	86.52	6.526	S
20	A	72.58	6.192	0.000
	B	87.56	5.568	S
30	A	71.21	5.250	0.000
	B	88.76	8.432	S
40	A	71.33	5.113	0.000
	B	89.36	5.773	S
50	A	73.88	7.249	0.000
	B	88.80	8.190	S
60	A	76.96	5.797	0.000
	B	88.28	6.967	S
90	A	77.88	5.773	0.000
	B	89.44	7.377	S
120	A	77.42	5.315	0.000
	B	90.20	6.151	S
150	A	79.12	5.944	0.000
	B	89.04	6.242	S
180	A	80.75	6.576	0.000
	B	89.76	6.502	S
240	A	80.79	6.086	0.000
	B	88.48	6.545	S
300	A	78.92	6.467	0.000
	B	88.52	4.464	S
360	A	80.33	7.257	0.000
		89.08	B 6.137	S

NS – Not significant ; S – significant

At base line the mean diastolic blood pressure (mm/Hg) it is observed there is no significant (P>0.05) difference between the groups. But the significant (P>0.05) difference is observed between the groups from time point 10 minutes to 360 minutes. In most of the time points the mean diastolic blood pressure (mm/Hg) is significantly higher in group B(control) compared to group A(study).

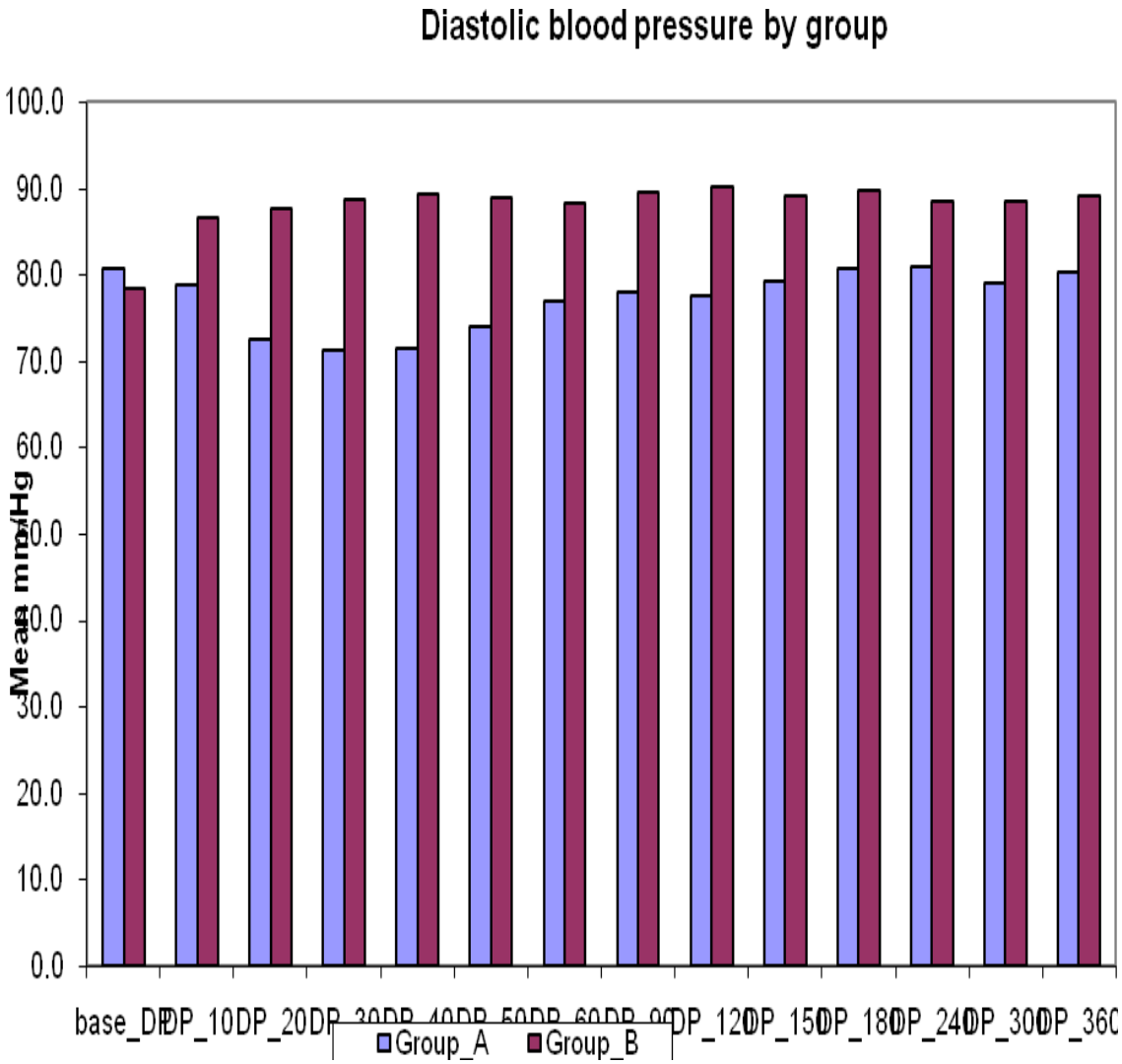
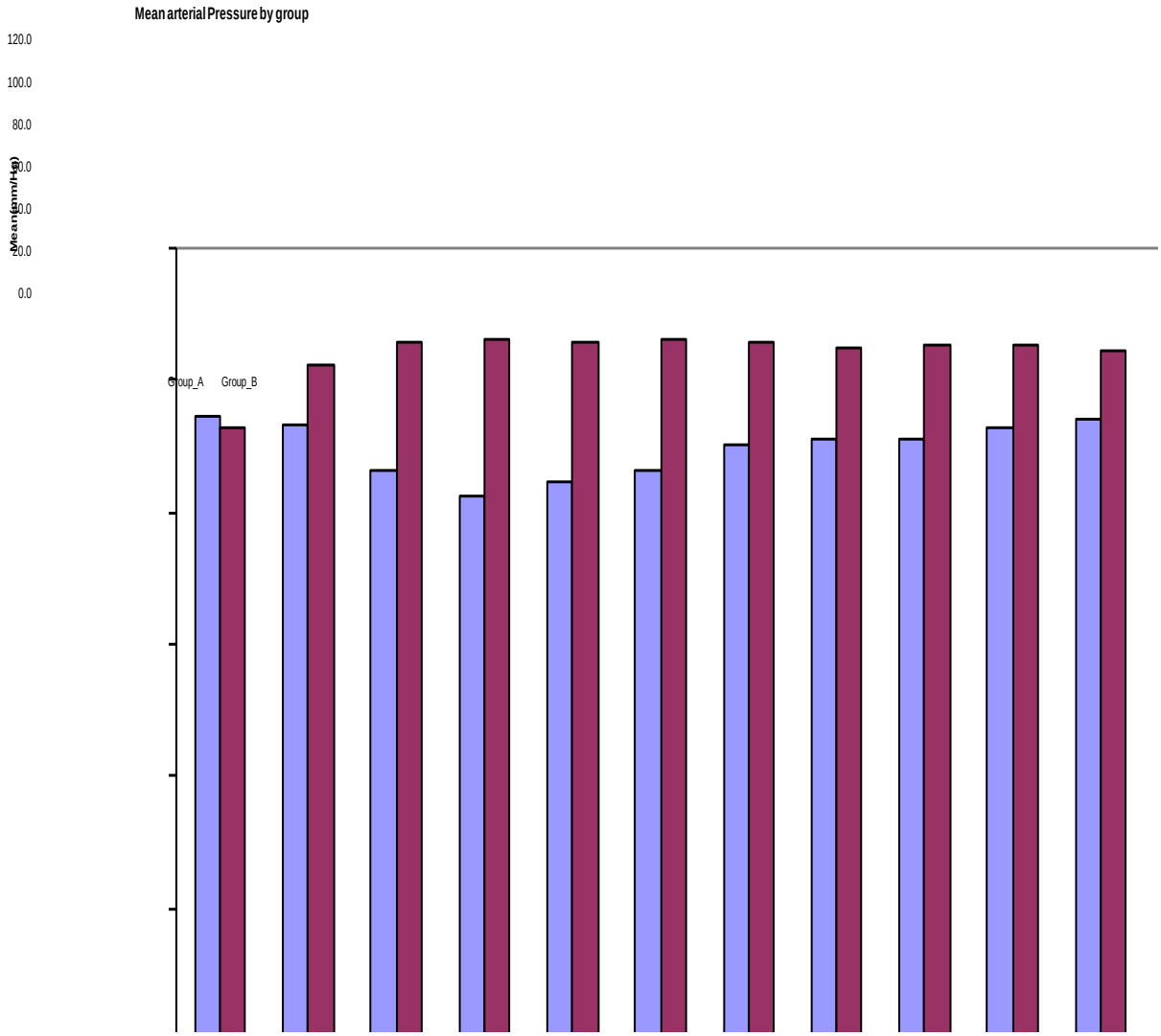


Table -7

Mean arterial pressure changes in the postoperative period by groups

MINS	Group	MAP Mean	Std. Deviation	P-value
Baseline	A	94.38	8.632	0.566 NS
	B	92.84	9.864	
10	A	93.21	8.954	0.001 S
	B	102.36	9.371	
20	A	86.33	7.287	0.000 S
	B	105.68	8.697	
30	A	82.38	5.717	0.000 S
	B	106.36	7.879	
40	A	84.71	7.068	0.000 S
	B	105.84	7.728	
50	A	86.29	7.092	0.000 S
	B	106.12	6.990	
60	A	90.04	7.997	0.000 S
	B	105.56	6.696	
90	A	91.04	7.006	0.000 S
	B	104.72	8.556	
120	A	91.00	5.816	0.000 S
	B	105.36	7.314	
150	A	93.00	6.757	0.000 S
	B	105.52	7.001	
180	A	94.12	6.516	0.000 S
	B	104.52	7.338	
240	A	94.42	7.144	0.000 S
	B	104.76	7.623	
300	A	94.29	6.695	0.000 S
	B	105.68	8.112	
360	A	94.00	6.345	0.000 S
	B	105.20	8.559	

At base line the mean arterialpressure (mm/Hg) ,it is observed there is no significant (P>0.05) difference between the groups. But the significant (P>0.05) difference is observed between the groups from time point 10 minutes to 360 minutes. In all the time points the mean arterial pressure (mm/Hg) is significantly higher in group B(control) compared to group A.(study)



Respiratory rate changes in the postoperative period by group at different time points

MINS	Group	RR Mean	Std. Deviation	P-value
20	A	14.96	1.628	0.064 NS
	B	14.16	1.313	
30	A	15.96	1.429	0.002 S
	B	14.56	1.609	
40	A	15.29	1.334	0.000 S
	B	14.04	.978	
50	A	15.83	1.810	0.006 S
	B	14.44	1.609	
60	A	15.50	1.694	0.100 S
	B	14.68	1.725	
90	A	15.12	1.941	0.809 NS
	B	15.24	1.332	
120	A	15.83	1.606	0.873 NS
	B	15.76	1.589	
150	A	16.79	1.444	0.072 NS
	B	16.08	1.256	
180	A	16.50	1.694	0.100 NS
	B	15.68	1.725	
240	A	15.67	1.659	0.913 NS
	B	15.72	1.720	
300	A	15.38	1.135	0.124 NS
	B	14.80	1.414	
360	A	15.12	1.393	0.245 NS
	B	14.60	1.708	

At base line the mean respiratory rate, it is observed there is no significant (P>0.05) difference between the groups. But the significant (P>0.05) difference is observed between the groups from time point 30 minutes to 50 minutes. Later on ,it is found that no significant (P>0.05) difference between the groups up to 360minutes. Though it is significant at time points 30,40,50 minutes, it is observed that invariably mean respiratory rate is significantly lower in group B(control) compared to group A(study).

The need for rescue analgesia by groups

Group	**Rescue_analgesia**		
	No	**Yes**	**Total**
Group_A	24 100.0%	0 .0%	24 100.0%
Group_B	15 60.0%	10 40.0%	25 100.0%
Total	39 79.6%	10 20.4%	49 100.0%

P=0.001

The proportion of need for rescue analgesia in group B(control) is 40.0% which is significantly higher compared to groupA(study) .In fact , this proportion is nil in group A. There is a statistical significant (P<.05) association between the need for rescue analgesia and the groups. None of the patients in group A (study group) required rescue analgesia.

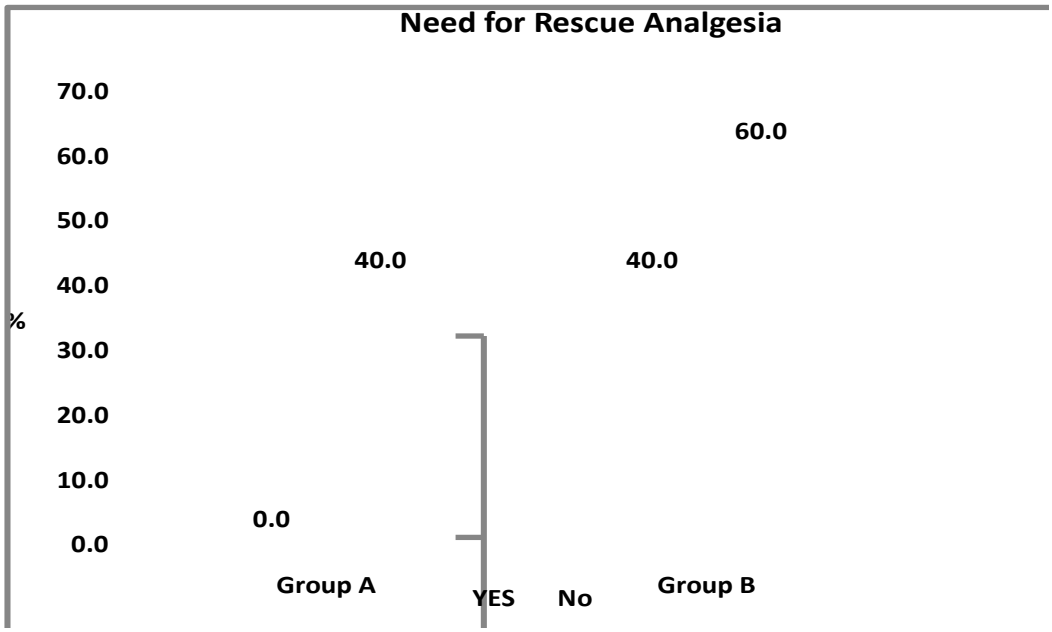


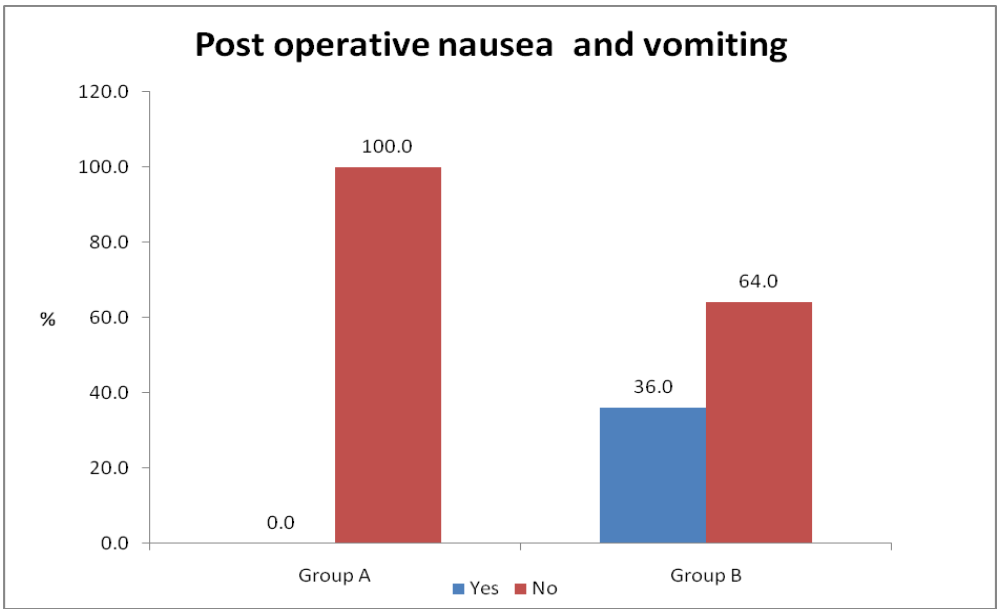
Table -9

PONV by Group

Group	PONV		
	No	**Yes**	**Total**
Group_A	24 100.0%	0 .0%	24 100.0%
Group_B	16 64.0%	9 36.0%	25 100.0%
Total	40 81.6%	9 18.4%	49 100.0%

P=0.002

The proportion of PONV in group B(control) is 36.0.0% which is significantly higher compared to groupA(study) .In fact , this proportion is nil in group A. There is a significant (P<.05) association between PONV and the groups.



DISCUSSION

The aim of the study was to study the effectiveness of thoracic paravertebral block versus systemic opioids for relief of postoperative pain in patients undergoing mastectomy under standardized general anaesthesia in both the groups.

Preethy J. Mathew et al in her study concluded that concentration of bupivacaine (0.25%) is as effective as bup ivacaine (0.5%) for relief of postoperative pain in mastectomy patients. This had the added advantage of lower incidence of toxicity profile. This was also confirmed by Ross. R.A. et al in his study. Hence, we used 0.25% bupivacaine in our study.

The mean age of group A(study) was 40.92 and mean age of group B(control) was 41.32. Hence, both groups were similar with respect to age.

The mean body mass index of group A(study) was 20.9. The mean Body mass index of group B(control) was 20.8. Hence, both groups were similar with respect BMI.

In our study the mean time duration to onset of complete analgesia in group A(study group) is 41.3 minutes and in group B(control group) is 31.2 minutes which is statistically significant.Sabyasachi Das et al in his study

found out that the mean time duration to onset of complete analgesia was 40.5 minutes in the paravertebral group compared to opioids (33 minutes) which is in concordance with our study.

In our study the mean time duration of complete analgesia (VAS score of zero) in group A(paraveretebral group) is 70 $\pm$ 43..2 minutes and in group B (systemic opiods) is 35.5 $\pm$ 8.678 minutes which is statistically significant. Sabyasachi Das et al in his study found out that the duration of complete analgesia in thoracic paravertebral block group patients is 67 minutes and in the opioid group is 34 minutes which correlates with our study.

The mean time duration of effective analgesia (VAS $\leq$ 4) in group A (Thoracic paravertebral block) is 308.71 minutes and in group B (systemic opioids) is 144.26 minutes. The time duration of effective analgesia is statistically sufficiently higher in Group A. This is in accordance with the study by sabyasachi Das et al who found out that the duration of effective analgesia in thoracic paravertebral block group was 295 minutes and 162 minutes in the opioid group. Hence, the mean time duration of effective and complete analgesia is significantly higher in the paravertebral group.

A study was conducted by Mukhorjee et al which also showed that the duration of effective analgesia afforded by TPVB was 344 minutes and 132 minutes in the opioid group. This finding correlated with our study.

In our study, the baseline pulse rate, respiratory rate, systolic and diastolic blood pressures, mean arterial pressure were found to be comparable. However, at every time the vitals were monitored the hemodynamic variables were much closer to the preoperative values and showed greater stability in the paravertebral block group (group A) compared to group B (Injection Tramadol 100 mg intravenously).

This is in concordance with the study by Jerzy A. Palaeczy who found out that thoracic paravertebral block in open cholecystectomy significantly improved hemodynamic parameters.

The need for rescue analgesia in TPVB patients when compared to systemic opioids is nil in our study. This is in concordance with the study by sabyasachi das et al who published similar results.In his study the need for rescue analgesia in the thoracic paravertebral block patients was 4% and 21% in the opioid group which was statistically significant.

The incidence of postoperative nausea and vomiting was nil in thoracic paravertebral block group in our study. However, nine out of 25

patients in group B(control) had PONV . This is in concordance with the studies of S.M. KLEIN who published similar results.He reported an incidence of 4% PONV occurrence in thoracic paravertebral block patients compared to an incidence of 36% in patients receiving opioids..

There was no incidence of bradycardia in either of the groups. There was no incidence of hypotension in either group which is in accordance with the study by Preethy J. This is reasonable given the fact that the concentration of Bupivacaine was only 0.25% and the blockade is unilateral and limited to a few dermatomes (T2-T6).Other side effects like pruritis,allergy to drugs ,pneumothorax were not reported in any of the groups.

SUMMARY

We conducted a randomised,controlled trial in a group of 50 patients who belonged to ASA class one and two undergoing elective mastectomy under general anaesthesia to compare the hemodynamic stability and postoperative analgesia between thoracic paravertebral block and systemic opioids.50 patients posted for modified radical mastectomy were randomized to receive either thoracic paravertebral block or systemic opioids.All the patients were given blocks by the same anaesthesiologist.

1. The mean time duration to onset of complete analgesia in group A(study group) is 41.3 minutes and in group B(control group) is 31.2 minutes which is statistically significant.

2. The mean duration of complete analgesia(VAS score of zero)in group A(study group)is 70 minutes and in group B(control group) is 35.5 minutes which is statistically significant.Hence the time duration of complete analgesia is significantly higher in the thoracic paravertebral block patients.

3.The mean time duration of effective analgesia(VAS<4) in group A(study group)is 308.71 minutes and in group B (control group) is 144.26 minutes which is statistically significant.Hence the time duration of effective

analgesia is significantly higher in thoracic paravertebral block group (group A).

4. The need for rescue analgesia in group A(study group) is nil,while in group B(control group)seven out of twenty five patients required rescue analgesia.

5. The incidence of PONV in group A(study group)is nil,while in group B(control group),ten out of twenty five patients reported PONV.Hence,the incidence of PONV is significantly lower in thoracic paravertebral block group.

CONCLUSION

This study concludes that thoracic paravertebral block provides a better postoperative analgesia,stable hemodynamic status,,nil incidence of postoperative nausea and vomiting,and overall better comfort for the patients undergoing mastectomy under general anaesthesia than systemic opioids.(injection tramadol)

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PROFORMA

TO STUDY THE EFFECTIVENESS OF THORACIC PARAVERTEBRAL BLOCK VERSUS SYSTEMIC OPIOIDS FOR RELIEF FOF POST OPERATIVE PAIN IN PATIENTS UNDERGOING MASTECTOMY UNDER GENERAL ANAESTHESIA IN RANDOMLY SELECTED ELECTIVE ADULT SURGICAL PATIENTS

NAME : AGE : SEX : I.P. No :

DIAGNOSIS : SURGERY PLANNED :

PREOPERATIVE ASSESSMENT :

HISTORY:

CO-MORBID ILLNESS & TREATMENT DETAILS :

EFFORT TOLERANCE - _____ METS

H/O PREVIOUS SURGERY :

GENERAL EXAMINATION :

HEIGHT : WEIGHT : BMI :

ANAEMIA JAUNDICE - SPINE –

PULSE - BP- CVS –

RS-

INVESTIGAIONS :

Hb : BT : CT :

BLOOD GROUPING & TYPING :

BLOOD SUGAR : UREA : CREATININE :

ECG : CXR :

PARAVERTEBRAL BLOCK:

SPACE	NEEDLE	SIZE	APPROACH	POSITION	DRUG

ANALGESIA BY V.A.S:

TIME TO REACH V.A.S. = 0	
COMPLETE ANALGESIA	
EFFECTIVE ANALGESIA	

VITAL PARAMETERS :

TIME	PR	SBP	DBP	MAP	RR	SIDE EFFECTS
Base line						
10 min						
20 min						
30 min						
40 min						
50 min						
60 min						
90 min						
120 min						
150 min						
180 min						
4 hrs						
5 hrs						
6 hrs						

SIDE EFFECTS :

Side effects	
Hypotension	
Brady cardia	
PONV	
Need for rescue analgesia	

INJ.EPHEDRINE (6 mg iv bolus) :

INJ.ATROPINE (0.6 mg iv bolus) :

RESCUE ANALGESIA :

PATIENT CONSENT FORM

TO STUDY THE EFFECTIVENESS OF THORACIC PARAVERTEBRAL BLOCK VERSUS SYSTEMIC OPIOIDS FOR RELIEF FOF POST OPERATIVE PAIN IN PATIENTS UNDERGOING MASTECTOMY UNDER GENERAL ANAESTHESIA IN RANDOMLY SELECTED ELECTIVE ADULT SURGICAL PATIENTS

Study Centre : Department of Anaesthesiology & Critical Care, Kilpauk Medical College.

Participant Name : Age : Sex :

O.P. No :

I confirm that I have understood the purpose of procedure for the above study. I had the opportunity to ask the question and all my questions and doubts have been answered to my satisifaction.

I have been explained about the pitfall in the procedure and the management of it. I have been explained about the safety, advantages and disadvantages of the techniques.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study.

I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study of “to study the effectiveness of thoracic paravertebral block versus systemic opioids for relief of post operative pain in patients undergoing mastectomy under general anaesthesia in randomly selected elective adult surgical patients”.

Name of the patient : Signature / thumb impression of patient :

Name of the witness : Signature :

Address : Contact Number :

Name of the Investigator : Signature :

Time : Date :

Place :

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.4098/ME-1/Ethics/2012 Dt:07.06.2012.
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College , Chennai reviewed and discussed the application for approval entitled "To study the effectiveness of thoracic paravertebral block versus systemic opioida for relief of pst operative pain in patients undergoing mastectomy under general anaesthesia".submitted by Dr.L.Sanjiv, MD (Anaesthesiology), PG Student, KMC, Ch-10

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
27 JUL 2012
Kilpauk, Chennai-10.

27/7/12
CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

s.no	name	ip no	age	bmi	asa	failure	complete analgesia in min	e. analgesia in min	need for rescue analgesia	ponv
1	selvi	32416	34	22.3	two	no	40	324	no	no
2	valli	34562	42	25.6	two	no	54	278	no	no
3	lakshmi	34567	46	23.1	two	no	42	297	no	no
4	priya	35621	37	21.5	two	no	47	299	no	no
5	rathi	37823	34	19.8	two	no	35	364	no	no
6	anjali	35647	46	19.9	two	no	47	334	no	no
7	rosy	35712	42	21.7	two	no	39	311	no	no
8	chitra	31121	45	20.3	two	no	38	264	no	no
9	kuppu	32468	39	22.6	two	no	51	312	no	no
10	umarani	31122	41	20	two	no	34	345	no	no
11	malliga	34579	45	21.2	two	no	41	256	no	no
12	usha	37854	46	19.3	two	no	46	317	no	no
13	nithya	42361	47	22.4	two	no	43	321	no	no
14	monica	31254	29	19.4	two	no	34	289	no	no
15	priyanka	32111	34	20.6	two	no	50	344	no	no
16	asha	30112	47	20.5	two	no	44	311	no	no
17	ramya	35634	39	21	two	no	33	332	no	no
18	asitha	32222	41	19.9	two	no	45	340	no	no
19	sridevi	31122	43	23	three	no	52	278	no	no
20	thilaga	32110	41	22	two	no	35	266	no	no
21	srividya	38631	42	19	two	no	50	318	no	no
22	chandika	38889	40	19.7	two	no	42	278	no	no
23	baby	34457	38	20	two	no	61	332	no	no
24	ranjini	31123	56	20		yes				no
25	sneha	36879	44	19	two	no	48	299	no	no

s.no	baseline PR	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	78	80	83	76	81	83	85	82	85	90	93	91	88	90
2	83	85	89	85	80	84	89	88	92	91	88	82	83	81
3	78	80	83	81	79	73	78	82	81	83	89	91	82	79
4	86	89	92	93	84	82	84	87	89	87	94	93	84	87
5	90	92	94	90	88	84	83	85	87	88	93	88	90	91
6	75	78	76	82	78	84	72	83	80	87	88	78	73	76
7	79	80	83	84	81	78	82	83	88	91	93	82	78	80
8	72	76	80	79	80	74	76	71	79	86	82	80	75	73
9	75	77	80	78	74	76	80	88	89	78	75	76	78	80
10	80	83	85	83	80	88	83	86	90	93	83	80	84	85
11	83	87	85	88	85	83	82	85	88	90	84	88	83	80
12	74	74	76	79	80	74	72	74	80	86	90	85	73	76
13	81	85	84	87	82	78	79	83	83	87	85	88	79	84
14	95	97	100	101	99	93	89	90	91	98	107	97	93	98
15	86	89	90	93	87	83	86	88	83	82	90	93	90	87
16	79	80	87	89	83	76	79	80	83	88	93	89	84	80
17	80	87	89	83	76	79	80	83	88	93	89	84	87	80
18	84	82	84	84	89	82	81	87	92	102	100	91	88	91
19	75	77	79	83	78	81	76	79	83	87	91	81	73	73
20	79	83	87	83	86	89	92	94	94	104	111	103	88	93
21	86	90	93	92	98	101	93	95	98	100	101	97	94	91
22	84	89	87	86	89	84	81	83	81	88	91	86	84	87
23	91	93	98	101	89	94	96	93	99	100	98	97	95	93
24	78	75	84	81	85	80	81	89	93	97	84	75	79	80

s no	baseline sbp	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	180 mins	4 hrs	5 hrs	6 hrs
1	112	121	119	115	104	98	103	109	110	106	114	117	113	115
2	121	120	115	109	105	104	112	114	117	124	127	128	125	120
3	126	121	110	116	112	115	118	125	122	126	128	123	125	126
4	125	121	110	116	112	115	98	114	117	120	123	118	115	110
5	102	105	98	95	96	98	101	104	100	99	104	102	107	102
6	130	134	116	96	110	118	121	125	120	125	130	133	127	124
7	125	121	110	106	113	121	126	127	120	128	123	119	122	125
8	133	136	125	117	111	115	116	120	128	127	123	119	122	125
9	136	131	122	140	128	122	124	127	125	129	130	134	132	140
10	127	120	125	114	125	126	120	118	124	127	130	128	125	132
11	121	116	113	114	117	121	125	126	120	118	116	119	117	121
12	126	134	102	116	108	110	114	118	120	125	127	129	122	130
13	128	125	118	111	108	115	118	121	125	128	123	119	123	126
14	108	104	101	96	94	95	99	102	106	111	115	119	114	120
15	123	126	107	105	101	115	117	121	125	130	127	124	128	125
16	129	125	113	112	108	115	118	121	125	128	123	119	123	126
17	125	127	108	110	105	103	116	118	122	125	128	125	129	130
18	117	110	108	102	103	127	121	125	127	116	119	125	124	128
19	126	124	106	117	108	116	114	115	120	124	127	125	123	127
20	105	98	95	99	103	110	102	105	110	113	116	102	110	105
21	103	95	90	92	98	95	106	102	105	110	111	114	107	104
22	118	123	120	112	114	102	112	120	122	118	115	114	117	123
23	124	121	103	107	105	114	115	118	125	121	119	126	117	118
24	134	130	112	121	118	116	123	127	126	124	119	123	127	122

s no	baseline dbp	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	180 mins	4 hrs	5 hrs	6 hrs
1	70	83	80	75	65	62	70	72	70	74	81	82	78	82
2	82	80	75	70	73	80	73	82	75	83	85	85	84	81
3	85	73	75	73	75	77	79	83	82	84	87	85	83	80
4	85	80	73	71	70	68	72	75	81	82	78	73	72	66
5	60	63	60	62	64	66	69	70	65	61	60	64	62	65
6	88	87	75	72	72	71	80	82	81	83	85	86	83	82
7	83	83	80	71	78	72	80	84	85	87	81	80	78	81
8	87	83	74	76	72	81	82	86	82	80	83	85	89	90
9	90	88	78	80	72	71	81	80	82	80	83	85	89	88
10	85	81	83	71	75	82	80	78	83	87	81	80	84	81
11	80	74	70	71	73	80	83	82	78	76	75	78	74	80
12	84	88	75	72	64	68	73	76	82	83	85	86	82	90
13	86	84	78	70	79	74	76	78	80	78	87	86	75	84
14	84	82	76	80	69	77	74	80	82	85	81	81	83	89
15	67	63	60	58	60	61	64	65	67	70	72	75	73	70
16	88	86	75	72	70	68	76	85	73	80	96	90	83	87
17	86	85	67	75	78	83	85	78	76	82	83	84	78	74
18	75	75	67	66	78	88	85	76	78	82	83	85	82	84
19	86	82	73	76	73	75	80	70	74	83	82	85	84	78
20	70	68	66	69	70	76	68	70	73	75	80	70	74	78
21	65	64	62	64	68	63	73	71	74	76	76	77	70	68
22	78	74	74	66	66	70	78	81	79	74	79	74	73	80
23	80	78	70	76	70	78	81	79	74	73	75	80	85	82
24	90	88	76	73	78	82	85	86	82	81	80	83	76	88

s no	baseline map	10 mins	20 mins	30 mins	40mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	84	96	93	88	76	76	74	83	85	82	87	93	95	90
2	95	93	88	83	87	91	87	96	89	97	99	99	98	94
3	97	89	87	86	91	87	96	89	97	99	99	98	94	94
4	98	94	85	83	71	78	86	82	89	94	96	81	91	87
5	74	77	73	73	73	76	79	80	78	74	73	77	75	78
6	102	103	94	79	88	87	94	96	94	97	100	102	98	96
7	97	96	90	86	83	88	95	98	97	100	95	93	93	96
8	102	105	97	88	93	95	100	96	93	97	100	103	105	102
9	105	102	93	89	94	93	96	96	98	101	102	104	99	105
10	99	94	97	85	88	89	96	93	91	97	100	101	99	96
11	94	88	84	85	88	94	97	97	92	90	89	92	88	94
12	98	103	89	78	84	84	81	87	90	95	97	99	100	95
13	100	98	91	88	89	92	92	95	97	98	94	95	97	100
14	81	77	74	71	71	72	76	77	80	84	86	90	87	95
15	97	99	86	81	88	89	94	97	101	98	95	99	99	92
16	102	99	88	92	80	86	99	90	88	103	100	97	99	100
17	99	99	80	87	89	95	97	99	91	90	99	91	100	100
18	89	87	81	75	96	92	97	99	91	90	96	97	99	92
19	99	96	85	79	82	79	83	87	87	94	97	99	96	97
20	82	78	76	79	81	87	79	82	85	88	93	81	86	90
21	78	74	71	73	78	74	84	81	85	87	88	89	82	80
22	91	94	92	84	89	84	92	95	92	88	87	89	94	90
23	97	94	88	78	83	87	88	91	98	95	93	99	93	92
24	105	102	90	87	91	96	99	99	96	94	94	98	96	101

s no	RR 20 min	30 mins	40mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	16	18	15	16	14	15	15	17	19	17	16	14
2	14	16	13	12	14	12	14	17	16	14	13	14
3	18	17	15	18	17	16	18	19	18	16	17	17
4	14	15	16	16	15	17	15	18	19	15	14	14
5	16	17	16	18	16	14	16	18	15	15	16	14
6	18	17	15	16	16	15	17	18	19	17	16	16
7	14	16	15	12	13	15	16	14	14	16	15	16
8	13	15	15	17	14	13	14	16	14	14	16	15
9	17	15	15	16	17	15	17	18	17	15	16	16
10	15	17	18	16	18	16	16	18	17	18	16	15
11	14	13	16	15	17	16	18	17	16	15	16	14
12	15	16	14	18	17	16	17	19	16	18	16	17
13	15	15	16	18	16	14	17	18	18	17	16	17
14	17	16	17	15	18	16	17	16	15	17	16	15
15	15	17	16	18	16	17	16	15	17	16	15	14
16	12	15	16	15	15	17	16	16	14	13	15	14
17	14	14	13	15	16	13	13	16	15	14	15	16
18	15	17	15	18	14	15	16	18	19	17	15	16
19	16	18	15	16	14	16	14	16	18	19	17	15
20	15	17	18	15	16	14	17	18	16	15	14	16
21	12	13	15	13	12	13	15	16	14	12	13	11
22	13	15	13	14	16	11	13	14	17	15	17	15
23	15	16	14	16	13	17	14	15	16	15	14	15
24	16	18	16	17	18	20	19	16	17	16	15	17

GROUP B OPIOIDS

S NO	NAME	IP NO	AGE	BMI	ASA	FAILURE	COMPLETE ANALGESIA	E ANALGESIA	RESCUE ANALGESIA	PONV
1	asha	34678	40	22.6	two	no	24	164	no	yes
2	priyamani	32277	52	19.3	two	no	19	133	yes	yes
3	madhuvani	30456	36	20.1	two	no	32	174	no	no
4	shailaja	32189	39	21	two	no	28	146	no	no
5	ammu	31122	46	20	two	no	34	132	yes	no
6	begum	26785	40	23.1	two	no	25	155	no	no
7	prema	35892	48	20.5	two	no	38	126	yes	no
8	gomathi	34211	33	19.4	two	no	26	160	no	no
9	mary	43678	42	25	two	no	31	136	no	yes
10	rakshita	35721	44	18.8	two	no	30	144	yes	no
11	mohana	32144	47	20.6	two	no	42	132	no	yes
12	geetha	36688	44	19.7	two	no	38	149	no	no
13	pramila	32417	34	23	two	no	27	116	yes	no
14	vairamala	31168	39	19	two	no	34	121	no	yes
15	kanaka	35672	34	19.9	two	no	29	160	no	no
16	preethi	30404	43	20.5	two	no	23	134	yes	no
17	riyanka	32244	51	20	two	no	21	117	yes	no
18	jessie	35667	42	19.8	two	no	36	174	no	yes
19	amsavalli	34210	37	22.4	two	no	32	153	no	yes
20	rekha	35568	45	20.2	two	no	39	112	yes	no
21	shilpa	34221	47	19.9	two	no	40	178	no	no
22	kokila	38907	34	23	two	no	29	122	yes	no
23	kalaivani	32146	42	21.7	two	no	32	154	no	yes
24	gayathri	37788	32	19.9	three	no	36	182	no	yes
25	kalyani	34668	42	20	two	no	34	132	yes	no

sno	baseline pR	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	76	94	102	104	108	82	88	74	87	100	112	114	108	106
2	80	104	122	102	98	66	64	106	98	102	84	102	100	82
3	78	100	102	100	100	98	97	99	96	100	101	102	102	98
4	86	62	70	64	58	70	62	68	80	64	62	66	62	68
5	90	78	72	66	122	112	108	74	78	62	74	70	70	82
6	74	88	92	94	96	92	100	98	112	100	88	98	96	80
7	80	112	104	102	100	106	98	92	102	98	92	108	104	112
8	66	88	94	92	90	98	100	98	92	94	90	90	88	94
9	76	102	100	110	104	106	102	112	98	94	88	80	86	102
10	74	98	100	94	102	92	94	88	100	98	96	92	90	106
11	83	96	104	106	112	114	100	98	102	103	101	100	98	99
12	95	76	79	74	70	78	81	74	70	81	79	76	69	72
13	81	109	112	106	99	100	114	102	104	100	98	103	101	106
14	78	96	96	92	104	98	92	90	114	94	98	84	100	102
15	79	97	103	105	101	105	98	99	101	99	97	101	97	97
16	79	91	87	99	103	102	93	99	100	103	105	100	111	103
17	72	88	96	94	92	98	100	86	94	98	102	89	92	94
18	86	110	102	104	106	97	103	102	100	103	102	101	106	102
19	91	73	76	80	72	79	72	78	73	71	69	74	77	75
20	90	117	121	109	104	106	112	103	115	106	108	102	113	109
21	74	88	92	96	92	98	96	90	94	97	100	100	106	98
22	86	104	112	107	98	94	102	97	95	89	103	105	107	103
23	70	87	91	97	94	92	100	99	91	93	91	96	92	93
24	82	91	88	97	98	102	103	102	100	100	98	96	98	98
25	84	92	98	100	102	98	100	92	112	106	100	98	94	92

s no	baseline sbp	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	114	142	136	128	140	138	142	146	148	134	138	122	130	128
2	123	146	140	138	134	142	144	138	146	144	138	142	132	130
3	125	144	142	138	126	132	134	136	137	132	138	133	132	139
4	132	112	102	106	98	114	109	102	107	103	102	111	121	134
5	134	121	116	102	106	104	102	108	123	127	138	146	154	112
6	109	138	142	144	134	137	149	135	137	136	132	138	132	132
7	121	127	112	102	136	138	134	139	112	129	112	101	142	144
8	117	138	137	102	117	119	121	129	137	131	136	134	138	`132
9	119	134	140	145	144	138	136	130	139	136	137	132	111	134
10	124	102	112	122	132	142	144	146	136	137	144	140	122	124
11	121	116	112	113	117	121	125	121	120	117	113	115	116	129
12	127	130	112	91	106	114	118	127	98	119	141	102	123	127
13	100	134	132	128	124	132	133	136	112	128	116	129	142	142
14	106	131	122	110	94	124	127	125	129	130	132	139	129	122
15	125	96	94	102	100	100	116	102	104	98	117	105	102	100
16	130	112	110	113	121	116	138	140	132	128	126	122	139	134
17	127	137	139	141	134	143	145	146	148	144	139	137	141	140
18	125	137	136	128	142	134	138	142	140	138	128	126	127	125
19	112	134	135	129	133	138	127	137	139	134	129	136	134	140
20	127	120	125	109	116	128	118	124	127	130	128	125	129	130
21	130	132	142	134	106	96	94	87	130	135	138	140	142	144
22	122	134	138	133	133	139	141	137	135	133	138	141	129	137
23	130	132	141	139	112	119	123	127	123	130	132	136	138	137
24	118	127	129	131	116	118	128	128	134	137	137	139	132	130
25	128	125	118	121	127	125	127	125	134	132	133	136	136	139

s no	baseline dbp	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	72	88	94	90	92	96	84	86	98	93	91	88	90	84
2	78	94	92	96	90	64	98	94	96	90	92	90	92	89
3	85	71	83	88	95	93	92	90	87	83	97	93	90	99
4	85	90	92	88	87	83	85	89	93	98	97	97	90	81
5	62	78	84	82	89	78	74	72	78	75	79	71	83	87
6	86	94	92	90	92	90	94	92	90	88	86	83	90	94
7	87	91	93	95	98	93	83	81	82	87	88	89	90	90
8	90	90	90	904	96	99	91	93	95	97	98	90	94	93
9	85	90	92	98	94	96	90	92	98	99	90	99	94	95
10	84	88	87	89	90	92	99	97	98	90	96	90	92	99
11	78	84	89	102	90	98	91	96	98	90	92	88	84	88
12	86	92	82	88	89	90	90	99	94	87	88	80	88	92
13	66	84	78	76	80	78	74	72	79	80	82	84	88	74
14	88	100	98	102	92	88	89	95	93	92	90	98	92	86
15	74	90	88	84	86	82	92	98	90	94	99	90	92	98
16	82	87	88	90	90	98	99	94	93	92	98	90	92	90
17	70	89	78	73	84	87	86	89	81	83	86	97	86	80
18	74	79	83	85	86	88	82	90	94	78	73	77	78	87
19	64	78	82	71	78	79	77	80	83	81	82	88	80	80
20	74	79	83	84	89	91	92	94	91	90	91	83	85	88
21	76	91	87	88	90	93	94	97	92	96	92	90	89	87
22	65	78	79	80	74	82	81	83	85	88	82	83	81	90
23	90	84	96	102	92	93	87	84	85	92	94	92	88	90
24	78	85	88	90	93	96	92	87	89	89	90	92	91	94
25	82	89	91	98	98	93	91	92	93	94	91	90	94	92

s no	baseline map	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	85	98	99	101	103	104	99	102	98	104	105	102	108	102
2	95	111	110	108	109	107	110	103	98	94	100	99	102	97
3	93	97	99	102	101	103	105	101	102	100	109	108	103	99
4	98	110	112	110	108	107	106	105	104	109	110	112	115	110
5	72	83	85	89	90	92	94	90	88	96	93	90	91	82
6	101	105	112	114	106	109	99	97	107	103	114	103	102	105
7	96	101	103	108	109	110	104	103	107	110	102	99	98	111
8	103	109	112	114	114	115	114	122	107	108	106	117	111	109
9	105	99	89	104	112	113	114	117	121	116	112	114	112	110
10	98	92	109	112	113	111	110	109	107	108	105	108	106	109
11	94	103	107	108	110	110	104	99	100	110	102	104	104	106
12	98	102	110	112	108	106	106	104	113	109	108	110	107	110
13	100	114	112	111	116	110	108	108	102	110	100	100	116	113
14	80	98	96	94	90	100	100	102	105	110	108	106	105	99
15	93	99	107	108	102	108	103	109	104	106	99	102	101	100
16	102	114	109	116	113	112	111	118	115	112	114	117	113	120
17	87	94	98	98	99	103	102	104	106	104	102	109	107	104
18	99	112	114	110	109	109	113	116	113	117	110	112	113	114
19	99	113	115	112	110	112	112	113	112	110	116	99	106	109
20	80	99	99	97	98	96	95	97	98	102	96	98	95	98
21	77	91	102	96	98	95	98	97	102	95	96	94	93	90
22	92	106	109	106	105	107	108	106	104	108	109	110	112	106
23	97	103	113	112	110	109	115	99	104	102	107	103	112	111
24	105	121	123	121	119	116	115	111	119	108	106	113	121	118
25	72	85	98	96	94	89	94	86	98	87	84	90	89	98

s no	RR 20 mins	30 mins	40 mins	50 mins	60 mins	90 mins	120 mins	150 mins	3 hrs	4 hrs	5 hrs	6 hrs
1	14	16	14	16	15	17	18	16	16	15	14	16
2	16	17	16	14	18	16	17	18	17	18	16	17
3	13	14	13	15	13	16	14	16	17	15	14	13
4	14	13	15	13	16	16	17	15	15	14	13	15
5	15	15	14	13	15	16	17	16	18	17	16	16
6	13	12	14	13	14	13	15	16	14	16	13	13
7	13	15	13	14	15	15	16	17	15	13	15	14
8	14	13	14	15	13	16	14	17	17	18	15	14
9	16	17	14	16	18	19	18	17	16	18	16	18
10	16	15	16	14	16	17	15	15	17	18	16	16
11	14	13	14	15	13	15	17	16	17	16	18	15
12	15	15	14	16	14	15	16	17	15	14	13	15
13	16	15	15	17	16	16	14	17	18	17	14	16
14	15	17	13	14	16	15	18	17	19	16	15	16
15	16	14	16	14	14	15	16	18	16	17	15	14
16	12	15	13	12	11	13	15	13	12	11	13	11
17	13	12	13	12	15	14	15	16	13	14	13	14
18	15	17	14	15	14	16	17	18	16	17	17	15
19	15	14	14	13	15	14	15	16	15	16	15	17
20	13	12	13	11	13	15	13	15	17	15	13	12
21	12	13	14	16	18	14	12	14	13	16	15	12
22	13	14	13	16	14	15	17	15	14	16	15	14
23	13	14	13	16	14	15	17	15	14	16	15	14
24	13	16	15	14	13	14	16	17	15	16	17	13
25	15	16	14	17	14	14	15	15	16	14	14	15